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BRITISH MEDICAL JOURNAL

LONDON SATURDAY MARCH 21 1953

CHANGING CONCEPTS OF HEALTH AND DISEASE, WITH PARTICULAR REFERENCE TO "PSYCHOSOMATIC MEDICINE"*

BY

R. R. BOMFORD, D.M., F.R.C.P.
Physician to the London Hospital

I do not think anything I shall say is new; much of it has been better said before, and some of it is very old—so old indeed that there always is a chance it may be mistaken for new. But I am encouraged to hope that, even so, it may fulfil the terms of the Bradshaw Trust, which states simply that a lecture shall be given in memory of Dr. William Wood Bradshaw on a subject connected with medicine or surgery.

As a starting-point I propose to try to put into words some ideas about the nature of disease which seemed to be taken for granted in the medicine I was taught nearly twenty-five years ago. It was assumed, so far as I could see, that there were things or entities called diseases which could be studied and treated as such, Some of these arose in and affected the mind, and were the province of psychiatrists. Others arose in and affected the body, and were the province of physicians, surgeons, and various specialists.

Diseases with physical manifestations could be divided into organic and functional. Organic diseases were regarded as real, objective, and the proper object of study by scientific medicine. They had physical causes, which either had been or would be elucidated as a result of increasingly thorough study by physical, chemical, and bacteriological methods. In the investigation of a disease the object was to find "the cause" and to deal with it. There was little or no interest in functional disorder. Functional symptoms seemed usually to be regarded either as invented or imaginary or as rather mysterious and discreditable states which in some way affected inferior personalities.

I do not think, as a student, I heard the word "psychosomatic," which is not surprising, for this actual word was apparently first used in 1926. Within a few years, however, it was suggested that certain physical diseases for which no satisfactory cause could be found, and which were becoming increasingly noticeable as important sources of disability, were psychosomatic in nature. This appeared to mean that the structural changes found in the body were caused by a disordered mind. This possibility was eagerly seized on by a few, but denied or ignored by the many who believed that real organic disease had little or nothing to do with the mind and would ultimately yield its secrets to the methods of physics, chemistry, and bacteriology.

Though stated baldly and perhaps oversimplified, I believe that is a fair summary of some of the main ideas about disease which were more or less taken for granted in the medicine I was taught. If any of my teachers should say they took nothing of the kind for granted, I can only say that this was what an average student gathered, not so much perhaps from what they said as from what they did not say. One saw, of course, that many of one's teachers did treat their patients as persons rather than as mere vehicles of disease, but I believe this was more an expression of humanity than an indication that they accepted such an approach as necessary to the understanding of disease.

Ideas Still Taken for Granted

I believe that some at least of the ideas I have outlined are still taken for granted by many persons engaged in academic medicine, by which for the purpose of this lecture I mean medicine as taught in undergraduate teaching schools. I will not waste time in defending this latter statement at length, but would refer to two recent articles by eminent teachers in undergraduate schools.

The one lists what he calls the five common causes of disease: inborn and inherited abnormalities; excess of a chemical agent in the environment; deficiency of a chemical substance; infection or infestation by viruses, bacteria, fungi, or animal parasites; and physical trauma. He thinks it possible that the important diseases of unknown aetiology, such as the rheumatic diseases, peptic ulceration, and ulcerative colitis, will turn out to be due to these same causes, acting singly or in combination, but entertains the "possibility that there exists a group or groups of diseases the causation of which we do not comprehend, or comprehend but dimly." His statement of what he calls the psychosomatic hypothesis—which is at least commendably brief—is that it "attributes disease to certain abnormal states of the mind." This hypothesis is then immediately dismissed along with that of focal sepsis as unworthy of serious consideration by scientific medicine. "The small amount of critically established fact," he says, "on

*The Bradshaw Lecture delivered before the Royal College of Physicians of London on November 6, 1952.

which these two hypotheses were based can probably be accounted for on the fact that the condition of any patient suffering from a chronic disease deteriorates when there is superadded infection or disturbance of the mind" (Pickering, 1950).

The other, speaking of the place of psychotherapy in the treatment of peptic ulcer, says: "In this connexion it should be recognized that, while many neurotics invent digestive disturbances, the ranks of genuine ulcer cases contain no higher proportion of neurotics than does the population at large. Most ulcer patients, indeed, are the reverse of neurotic. They may be anxious and worried, but they never invent symptoms, generally make light of their suffering, and rarely give up work unless the pain is intolerable" (Illingworth, 1952).

I would like to assure the authors of these in many ways admirable lectures that I have picked on theirs out of many others I could have chosen, not from any personal animosity, but simply because they happen to illustrate my thesis that certain ideas which seemed implicit in what I was taught are still current in academic medicine to-day.

I believe these ideas are almost without exception open to serious objections. I shall now examine some of them further, and in doing so review in an admittedly eclectic manner some papers which seem to me to illustrate changing ideas. In particular I wish to examine a common misapprehension that there is something called the psychosomatic hypothesis, which holds that abnormal mental states can cause physical disease. This will involve at least some reference to the idea of diseases as entities, to the idea of cause in medicine, and to the problem of the relationship between mind and body.

Diseases

It was and often still is assumed that there are entities called diseases which can be studied and treated as such. But, if we think about it, it seems obvious that we cannot observe diseases: we can only observe diseased persons during life or the mortal remains of diseased persons after death. Nosological classification may be a necessary convenience for purposes of orderly description, but we have come to think and often to act as if the states it describes exist as entities which can be studied and dealt with apart from the person who is diseased. One might almost feel one had to apologize for mentioning something so apparently trite and obvious were it not that much current teaching and action appears to be based on the opposite assumption.

Cause in Relation to Medicine

I have already said that it seemed to be assumed, when I was a student, that organic diseases had physical causes, and by this there was often implied a single cause. The cause of lobar pneumonia was the pneumococcus. The cause of cirrhosis was alcohol, and so on. The business of diagnosis was to find the cause of the disease, and the object of rational treatment was to remove it. When the cause was unknown, only symptomatic or empirical treatment was possible. I have perhaps laboured these illustrations to show that we really did seem to think in terms of single causes, though we cannot have gone very far in considering the implications of this view.

The idea of cause is a complicated one, and many people much better qualified to do so than I have written about it in relation to medicine. Howe (1934), for instance, speaking of the kind of examples of cause and effect I have just mentioned, says: "However, not one of these examples is truly a case of cause and effect. Not only is the effect produced in each case by the interaction of at least two antecedent events, but each of these antecedent events is produced by the interaction of another two. If we are to be accurate we must then recognize not 'a cause' but an endless multiplicity of causation, which is extremely confusing. There never is, in fact, 'a cause' but always 'a relationship.'" And a little later on he says: "It is to-day generally agreed in theory, although not always recognized in practice, that disease is essentially an interaction between seed and soil, in both of which there is a convergence of a sequence of related events, from the association of which the effect is developed."

What we can observe, he says, is a series of events connected and related through the medium of time, stretching back into the past and forward into the future. If a bus runs over my leg I may say that the impact of the bus is the cause of the fracture of my femur. More accurately, the event may be described as the intersection of two time-sequences in which the bus time-sequence crosses the leg time-sequence. "If we seek causes we find two causal time chains: what caused the bus to be where it was, and what caused the driver of the bus to do as he did; what caused the leg to be where it was, and what caused the leg eventually to heal. These are not truly to be regarded as being causes, but as a series of related time-effects."

Recently Strauss (1952) devoted the first of his Croonian Lectures to a discussion of causality in medicine. I am afraid that many of the ill-educated generation to which I belong may have found his philosophical arguments difficult to follow. But we cannot fail to appreciate his criticism of rigid causal relationships in medicine and to be convinced of the inadequacy of our search for single or "specific" causes of disease. I cannot, however, resist one or two comments.

"It is arguable," says Strauss, "that a pure paired cause–effect relationship exists at two levels only: the ethical and the mechanical." Of the pure paired cause–effect complex at the mechanical level he gives two examples: a person swallowing a large amount of arsenic by mistake—the cause—leading to acute gastritis—the effect; and a second example, a personal experience of his own, of the sudden protrusion of a lumbar intervertebral disk—the cause—leading to severe pain in the back and complete immobilization below the waist—the effect.

These examples of simple cause and effect at a mechanical level are then contrasted with an account of the possible factors—bacteriological, constitutional, sociological, and psychological—concerned in the development by a particular person of the mode of morbid behaviour which we call pulmonary tuberculosis. The contrast is instructive, but one is compelled to ask whether in the two examples cited the effect can really be attributed to a single mechanical cause. I would like, for instance, to know how the "mistake" (which Strauss agrees is an over-simplification) of swallowing the arsenic occurred, and I would suggest the effect might have been different had the subject by some odd but not impossible chance been a habitual arsenic eater with a tolerance to the drug, such as has apparently been observed in Styrian woodcutters. Should not the effect in this case again be regarded as resulting from the convergence of two sequences of events—what caused the arsenic to be where it was and to be swallowed, and what caused the person who took it to be susceptible to its effects?

A Personal Experience

The second example interests me, also on account of a personal experience. I too suffered from a pain in my back—in this instance a chronic pain over many years—severe enough to be a nuisance at times, but never incapacitating or bad enough to make me do anything about it. In the earlier years I supposed it was due to fibrositis, whatever that is, and encouraged my dentist to look for a source of focal sepsis, which he did not find. Some years later, when it was particularly troublesome in a humid

tropical climate, I supposed that constantly damp clothes and bedclothes had something to do with it. Later, after reading about psychogenic backache, I concluded this must be the whole explanation. Some months ago an *x*-ray film of the spine showed, I am told, conclusive evidence of an old and considerable protrusion of a lumbar intervertebral disk. Here, surely, was another example of direct mechanical cause and effect, and incidentally a vindication of the importance of searching for a single demonstrable cause for a symptom or group of symptoms, rather than indulging in the vague speculations of multiple aetiology.

But I am not so sure, for I believe that the protrusion of my disk was not entirely an accident; and, further, I have to account for the fact that I have for some time been practically free from pain, though I am assured that the actual disk lesion is unlikely to have altered.

Briefly—and if you will forgive some personal details—I believe the protrusion of my disk can be traced back to two what might be called parlour tricks. The first was to challenge my fellows to put their hands flat on the ground in front of them without bending their knees. This, the only faintly distinctive physical achievement I had, used to give me satisfaction, and was probably harmless. Unfortunately some years later, though I had never been able to jump anything, I discovered I could do what is known in gymnastic circles as a "neck roll." This consists in diving over some object, turning a somersault on a cushion or mat, and landing on one's feet again. It was a great success at Army mess nights and similar occasions. Unfortunately it involved a sharp flexion of the lumbar spine, and after a year or two I had to abandon it on account of increasing pain and stiffness in my lower back. I have little doubt this eccentricity was an important factor in the protrusion of my disk, and, of course, the story could easily be pursued further by inquiring why a clumsy and rather obese physician should have found it necessary to perform "neck rolls" at an age when such an accomplishment is not generally considered necessary—but I do not intend to follow it further on this occasion. I have said enough to indicate that I am fairly sure the protrusion of my disk was not a simple mechanical accident.

Once it was discovered I was given some back-extension exercises and advised to wear a lumbo-sacral support. This contrivance supports nothing except any abdominal protrusion which may be present, but is effective because it makes bending so uncomfortable that one ceases to bend. I persevered with the belt and the exercises for at most a week or two. I was virtually free from pain within a few days and have now learnt that I can remain so without the aid of the support or the exercises, so long as I do not habitually slump in chairs and car seats. When I do so slump, I get a slight return of pain. I have no doubt that for me "slumping," as I have called it, is a physical expression of certain emotional attitudes.

I have troubled you with this rather long personal anecdote because it seems to me to illustrate clearly the inadequacy of the idea of single causes. For you will see that if you were to ask me what was "the cause" of the pain in my back I should find the question difficult to answer.

What we call the cause of an illness is never strictly the whole cause, though it may be a necessary factor in causation in the sense that one would not have that particular illness without that particular factor. I would not have had the particular kind of pain in my back if I had not had a protrusion of an intervertebral disk. But the protrusion of the disk was simply one link in a chain of causation, and the pain, once it was understood, was relieved by fairly simple measures, which presumably left the disk lesion *in situ*.

It is worth noticing, perhaps, that the main difference between these two examples of the protrusion of a disk is that the first might be described as an acute illness and the second as a chronic. This is probably an example of a general difference, to which attention has often been drawn, as for instance by Ryle (1942). Whether or no the search for single or specific causes is ever justified on philosophical grounds, it has been more productive of results in acute than in chronic diseases. Medicine's greatest successes have been in connexion with acute disease and particularly acute infections. Where partial success has been achieved in the treatment of chronic diseases, as in myxoedema, diabetes, and pernicious anaemia, one must note that in each instance the patient is not cured, and our knowledge of the aetiology of the condition is still quite incomplete. Our ability to deal successfully with most chronic diseases has advanced much more slowly than in the case of acute ones, and it is possible that this is due, at least in part, to our undue preoccupation with single specific causes and direct mechanical cause and effect.

Aetiology in Relation to Medicine

Aetiology is defined in the *Oxford Dictionary* as "the science or philosophy of causation" and in *Dorland's Medical Dictionary* as "the sum of knowledge regarding causes." Strauss has described the substitution of the term "aetiology" for "cause" as no more than a resort to the magic of semantics in an attempt to escape from the fetters of rigid causality. But I believe that the change in words can be something more than semantic juggling, and may represent a change both in ways of thinking and in ways of acting, which is to be encouraged even though we are still far from a satisfactory concept of aetiology.

Ryle (1942), after quoting the definitions I have mentioned, continued: "It is well to insist on such definitions, for the discovery by Pasteur and the great pioneers in bacteriology of specific microbic agents of disease, and the recognition by others of specific chemical agents and specific deficiencies, have, until quite recently and contemporaneously with their immense benefits to medicine, had a peculiarly limiting effect upon the vision and the practice of many medical men, not excluding teachers. They have, in fact, compelled a neglect of the associated causal factors without which no disease can have its being. They have also fostered a belief in or search for single determining causes where none exist."

A paper by Halliday (1943) seems to me of particular value in that, though some difficult matters are perhaps oversimplified, the author outlines a concept of aetiology which seems to avoid obvious pitfalls and to provide a reasonable system of thought on which medical action can be based. In the space available I can do scant justice to this paper, which could with profit be read, pondered, and re-read by every teacher of medicine.

Cause in medicine, says Halliday, has usually been regarded in one of two ways; and he calls them the "mechanismic" and the "biological."

Mechanismic Cause

The word mechanism refers to a system of mutually adapted parts working together as a machine. Given the requisite preceding movement, the ensuing movement follows necessarily upon it, provided the machine is in working order. During the last three centuries, knowledge of the human organism in terms of mechanism increased progressively and the organism came to be regarded as if it were in actual fact a machine. If it failed to function properly, the cause of the breakdown was similar to that of a machine—that is, a fault in one or more of the component bits and pieces. The primary concern of medicine was to identify the fault, which might be viewed by any technique—for example, gastric ulcer, a structural fault; acidosis, a chemical fault; or hypertension, a physical fault—and to take appropriate action by interfering with the mechanism.

Some of the implications of mechanismic aetiology Halliday summarized as follows: (1) The human organism

is a machine composed of mutually adjusted parts working together. (2) Illness corresponds to breakdown in the machine. (3) The cause of illness (provided the patient has adequate food, air, and water) is something wrong—a fault, disease, lesion, imbalance, or abnormality—in one or more of the parts. (4) Medical action is confined to interfering with the mechanism by what is known as the appropriate treatment.

This mechanismic attitude has, of course, brought great advances. The criticism of it is not so much that it is wrong as that it is not enough. In particular it gives little or no guide to action in the prevention of disease, for it is concerned with how a patient is ill rather than why he is ill. One might add that while few doctors now take a purely mechanismic view, most patients do, hence the very great difficulty of giving them any reasonable explanation of functional symptoms. Say what we will, the patient believes there must be a fault in the mechanism somewhere —"the cause"—and an appropriate means of dealing with it—"the cure." One might also point out that the mechanismic idea of disease allows of no definition of health other than the absence of disease, which is plainly inadequate, for there is a great difference between "no disease" and health.

Biological Cause

Halliday explains what he calls the biological idea of cause as follows. "Illness is regarded, not as a fault in the parts, but as a *reaction*, or mode of behaviour, or vital expression of a living unit in response to those forces which he encounters as he moves and grows in time. Cause is therefore *twofold* and is to be found in the nature of the individual and the nature of his environment at a particular point in time." The environment, the totality of exterior circumstances, may be investigated by a variety of techniques—physical, chemical, bacteriological, psychological, and so on—and in this way split up for convenience into separate components which we may call factors.

That an aspect of cause is found in the individual person may not at first sight seem so obvious. It may be illustrated by pointing out that when two persons encounter the same environmental factor the behaviour of each depends on his characteristics. Suppose, for instance, that a weight of 2 st. falls equally on the legs of a man aged 30 and of his father aged 80. The son will probably develop a superficial bruise, and the father a fracture of both legs. Two men swallow water containing virulent typhoid bacilli. One who gives no previous history of typhoid fever responds ten days later by a morbid reaction whose features include fever, prostration, diarrhoea, etc. The other, who does give a history of previous enteric fever, shows no evident morbid behaviour. When an S O S is broadcast several million people may be quite unaffected, while one man falls down in a faint. In each of these imaginary but quite possible examples the environmental factor was certainly not the whole cause. An aspect of cause was present in the persons affected.

Some of the implications of biological aetiology were summarized by Halliday as follows: (1) The human organism, although composed of parts, may also be regarded as an integrated unit or living person. (2) Illness represents a vital reaction of a person to factors of the environment which he meets as he moves in time. (3) The cause of illness is therefore twofold—certain characteristics of the person and certain factors of the environment. (4) Medical action is concerned primarily with measures designed (*a*) to alter or prevent characteristics of the person known to be causal, and (*b*) to alleviate or remove factors of the environment known to be causal.

This biological attitude is, as Halliday points out, a *sine qua non* for effective prevention of disease and may be very important in treatment. One might add that it does make possible a reasonable explanation of functional symptoms, the reaction of a particular personality to factors in the environment, and it does make possible a concept of health other than in terms of "no disease." Halliday then summarizes the ideas underlying the phrase "the cause of the illness" as follows:

"(*a*) As regards the *illness*, the fields of observation and discourse are the features (signs and symptoms) of a mode of behaviour of an individual.

"(*b*) As regards the *cause*, the fields of observation and discourse are three—namely:

"(1) *The field of the person.* Under this heading are put the observations on the characteristics of the person before he became ill. These are innumerable, and may be noted in terms of any technique. They include, for example, age, sex, weight, height, bodily habitus, history of previous illnesses, history of illness in the family, blood pressure, menopause, intelligence, etc. The problem is to distinguish which of these characteristics may be regarded as relevant and causal.

"(2) *The field of the environment.* Under this heading are included observations on the factors of the environment which the person met at, or shortly before, the time he fell ill. The observations may be made in terms of any technique—e.g., physical (trauma, heat, cold, light), chemical (diet, poisons), bacteriological, and psychological (death of a loved person, failure or promotion, etc.). Such factors are innumerable, and the problem again is to determine which of them may be regarded as relevant and causal.

"(3) *The field of mechanism.* Under this heading are put observations on the 'bits and pieces' (structural, physical, chemical, psychological, etc.) which are set into action by the encounter and which ultimately bring about the particular mode of behaviour. The problem is to distinguish which of these are primarily involved."

And the three questions which he suggests one should attempt to answer about any illness are, of course, now quite well known: (1) What kind of a person was this before he took ill?—that is, which characteristics of the person are relevant and causal? The field of the person. (2) Why did he become ill when he did?—that is, which factors of environment are relevant and causal? The field of the environment. (3) Why did he become ill in the manner he did?—that is, which part contacted the factor and which bits and pieces by preceding movement and ensuing movement finally made manifest the particular mode of behaviour? The field of the mechanism.

It seems at least, from this brief review of what is meant by cause or aetiology in medicine, that we can never strictly think in terms of a single or specific cause of a disease. On this ground alone it appears unsatisfactory to suggest that abnormal mental states can in themselves cause physical disease.

Body–Mind Relationships, with Reference to the "Psychosomatic Hypothesis"

It was assumed, and I think still is, that diseases can arise in and affect the mind on the one hand, or can arise in and affect the body on the other; and we argue then whether disturbance in the mind may cause disease in the body. My excuse for venturing, with some trepidation and in however superficial and amateur a fashion, on a subject which has puzzled some of the best minds of every generation for well over two thousand years, must be that I believe it is impossible to practise or teach medicine without making some kind of assumption or taking for granted some kind of hypothesis about the relationship between what we call mind and what we call body. Many people do not, of course, consciously make any such assumptions. They take them over ready-made from teachers and textbooks. I should put it rather, perhaps, that our attitude to disease and our manner of dealing with patients must involve some hypothesis of body–mind relationships, whether we are aware of it or not. Fortunately the problem I want to discuss is a fairly limited one. It is simply to ask, have we any right to divide diseases into physical and psychological, in the sense that they arise in the body or arise in the mind, and have we any right to talk about events in the mind causing disease in the body?

Monism

Victorian materialism regarded matter as real and objective, and mind simply as some kind of a by-product of matter. Though, so far as can be seen from their medical writings, this is the view to which many medical scientists still adhere, others adopt some kind of psycho-physical parallelism or some form of monism, which regards mind or conscious states and brain states as different aspects of the same events. As Russell Brain (1951a) explained one form of this hypothesis: "What we call events in the physical brain are happenings about which we may have indirect knowledge inferred from our perception of other people's brains and what they tell us about their experiences; but we have direct awareness of the physical events in our own brains and when we thus perceive them we find them to be thoughts, sensations, feelings, and so on."

According to this hypothesis there is thus only one kind of events, but they appear different to us because we have knowledge of our own minds in terms of perceptual symbols and knowledge of the physical world, including other people's brains, expressed in conceptual symbols.

If for the moment we accept this hypothesis, then it seems to me that the questions I asked have little meaning. Brain states and mind states are two aspects of one series of events which appear different only because we perceive them in different ways. One cannot then imagine purely physical disease or purely psychological disease, and it makes no sense to ask whether mental states can cause physical states. If one asks whether emotions like anxiety or anger can cause physical disease—what one is really asking is whether mind–brain states like anxiety or anger can cause physical disease elsewhere in the body. If, indeed, we watch someone losing his temper, can we really say that this is something in the mind—something purely mental—causing something in the body? And I do not think it makes much difference to the argument if we suppose that brain states and mind states are different events, but events moving, so far as we know, exactly in parallel.

Common-sense Dualism

I would like to ask those who talk about physical diseases arising in the body and psychological disorders arising in the mind, and who argue whether disorder in the mind can cause physical disease in the body, to explain to what kind of a hypothesis of body–mind relationships they are subscribing? So far as one can see, it must be a so-called common-sense dualism, which conceives of an independent immaterial mind in some mysterious way interacting with a material brain and body. But I suspect that this popular dualism again depends on the two kinds of knowledge to which Russell Brain (1951b) has drawn attention. We have difficulty in equating events in our own minds which we perceive directly as thoughts and feelings with events in brains of which we have only indirect knowledge by inference, and we therefore regard our thoughts and feelings as more or less independent things, without pausing to consider the implications of this view.

But whatever ultimate belief or philosophical hypothesis we may entertain, so far as our observation can go, a person is surely a body–mind unity. We have no experience of mind separate from body in ourselves, and we cannot imagine such a state of affairs in anyone else. So far as our own observations and the inferences we can make from them go, a person is a body–mind unity; body and mind are in some way inseparable aspects of a person.

It would seem, therefore, that we must regard all diseases as states or modes of behaviour of a person who is a body–mind unity, and it follows, surely, that all disease must be regarded as psychosomatic, in the sense this word is generally used. All disease must affect in some degree both body and mind. We have no right, then, to divide diseases into physical and psychological, in the sense of that which arises in or affects the mind and that which arises in or affects the body, nor to say that something happening in an entity mind can cause something else to happen in an entity body.

But we can study diseased persons by different methods. If we study them by methods which provide information in physical terms, we obtain information in physical terms. If we study them by methods which give an answer in psychological terms, we obtain information in psychological terms.

What we can do then is to group disease states roughly into those in which most of the relevant and useful information seems at present to be obtained by physical methods; those in which most of the relevant and useful information seems at present to be obtained by psychological methods; and those in which both methods supply relevant and useful information. The last group corresponds, of course, to what are often now referred to as the psychosomatic disorders.

But even this division can be no more than a rough and temporary grouping for the sake of convenience. For I believe it is true that the more diseased persons are studied by both physical and psychological techniques, the more disease states we find in which both methods produce relevant information.

Literature of "Psychosomatic Medicine"

The literature of so-called psychosomatic medicine—I shall come back to that term later—is already considerable, and I shall not attempt to review more than a very little of it, partly because such an attempt would need to occupy at least several lectures, and partly because I believe it would be unprofitable. For I suspect that a person's attitude to what may be called the psychosomatic method in medicine depends less on an intellectual evaluation of the literature than on his attitude to neurosis. Just as an overtly neurotic patient tends to arouse irrational feelings in most of us, so does the suggestion that illness, needless to say in ourselves as well as in our patients, can be fully explained only when psychological and physical factors are taken into account. We resist this suggestion as applied to ourselves, and we tend to deny it in our patients.

Earlier I quoted an article by Pickering (1950) in which he dismissed what he called the psychosomatic hypothesis in a few lines on the ground that the small amount of critically established fact on which it was based could be explained in other ways. But in doing this he makes an assumption: he assumes, it seems to me, that a satisfactory account of the causation of disease states, or some of them, has been, or can be, given in purely physical terms; and that it therefore behoves those who are interested in the so-called psychosomatic hypothesis to prove their case by providing critically established fact.

But this is a big assumption, and I would ask those who make it to consider carefully in how many chronic diseases can they give a satisfactory account of the aetiology in purely physical terms? We come nearest to giving such an account, I suppose, in nutritional deficiencies and in certain chronic infections, where again one factor in the environment is of particular importance. But is that factor, even in these instances, the whole story? A great deal is known, for instance, about the tubercle bacillus; but can we really explain on humoral grounds why some people become ill with tuberculosis while others do not, and, of those who do become ill, why in some the process is arrested while in others it is not? I doubt if we can, and I believe that studies of personal factors which may be concerned in the onset and course of tuberculosis such as those of Wittkower (1949) and of Day (1951, 1952), even though they do not amount to "critically established fact," are still of great interest and importance in this connexion.

I would like to suggest that we may equally, and indeed with much more reason, start from the historically older and philosophically more satisfactory assumption that illness

is a state of the whole man—in the sense that it is a state of a body–mind unity, and ask those who doubt the importance of psychosomatic method to establish their case by giving a satisfactory account in purely physical terms of the aetiology of even one of the chronic conditions which are at present described as of unknown aetiology. Peptic ulceration, ulcerative colitis, hypertension with all its sequels, rheumatoid arthritis, and asthma, to name but a few, await such an explanation.

But, it may be said, since rheumatoid arthritis can now be dramatically if not completely relieved by supplying the substance cortisone, we can surely regard rheumatoid arthritis as a purely physical abnormality, curable by physical means. And doesn't this make the complicated and difficult psychosomatic approach unnecessary?

Those who use this kind of argument are confusing mechanism with aetiology. The discovery of cortisone and A.C.T.H. has brilliantly illuminated, or bids fair to illuminate, the physico-chemical mechanism of rheumatoid arthritis amongst other things, but it has brought us no nearer being able to answer the question why a given person is taken ill with rheumatoid arthritis or how this illness can be prevented—just as the discovery of insulin and vitamin B_{12} has led to very great advances in our knowledge of the physico-chemical mechanism of diabetes and pernicious anaemia without telling us why some people develop these conditions or how they may be prevented.

Medicine in undergraduate teaching schools, as Halliday put it, has shown hitherto a distinctly mechanismic bias, in the sense that it has devoted enormous energy to the explanation of the mechanism of disease in physico-chemical terms, relatively less to the environment, and still less to the person. But there are signs that this is changing. There have been, for instance, numerous psychological studies of personality types in different illnesses, notably the very extensive contributions of Dunbar (1943), and her colleagues from the psychiatric and medical divisions of Columbia University. My own feeling is that these and other personality studies, though of great interest, are somewhat inconclusive in that they seem to depend so greatly on the subjective interpretations of the observer, and it remains to be seen whether independent observers will always find the same personality types or range of types in the same illnesses. At the same time a start has been made on the more accurate study of physical types by means of Sheldon's method of somato-typing (Tanner, 1949).

To my mind the outstanding recent contribution to the study of man, rather than mechanism, has been the work of Wolf, Wolff, and their colleagues at Cornell University Medical College, over the last 10 to 15 years.

For details of their methods and results one must read at least their two monographs (Wolf and Wolff, 1943; Grace, Wolf, and Wolff, 1951). Very briefly, one patient with a gastrostomy and four with prolapsed colonic mucosa were studied over considerable periods. The rate of blood flow, as judged by colour changes in the mucosa, and secretory and motor activity of the stomach and colon were measured in a variety of circumstances, and notes made on the effect upon them of ordinary physiological stimuli, of drugs, of the patient's particular life situation, and sometimes of emotionally coloured happenings, either occurring spontaneously or provoked deliberately during the course of the experiments.

I believe these are important studies for several reasons. They were performed on man, and intact man, except for the accident by which either gastric or colonic mucosa was visible. Instead of trying to standardize the conditions of their experiment by avoiding the complication of using conscious human subjects, or by what might be called eliminating the human factor, these observers standardized all the other conditions of their experiments so far as possible, and deliberately set out to study, among other things, the effects on the stomach and colon of human situations and emotions.

What emotion the subjects were actually experiencing in the different experimental situations had, of course, to be inferred. But, given that the authors' inferences were substantially correct, their results are of the greatest interest. I would like to mention one or two points which seem particularly relevant to my lecture. In an animal preparation the actions of a drug are usually constant and predictable. In these observations on man there are several instances where this was not so, and where the actual effect of a drug appeared to depend not on its pharmacological action but on the meaning of its administration to the particular subject. This is seen most clearly in the account of the effects of the intravenous administration of atropine on the colon in three of the subjects with colostomies. In two subjects who were thought to be in a state of relative security and relaxation the injections were accepted with apparent equanimity, and their effect was a profound decrease in motor activity of the colon and some blanching of the colour of the mucosa, as would be expected on pharmacological grounds. In a third subject, who resented the experiment, the same intravenous dose of atropine was followed by a great increase in motor activity and in the colour of the mucosa—changes which had been found previously in states of anger—and, though the atropine produced its expected effects on the salivary secretion and circulatory system, at no time was there any pallor or diminution in the motor activity of the colon. It appears that in this instance the physiological effect of the resentment aroused by the injection of the drug predominated over its expected pharmacological effect.

This observation is in fact a particular instance of something which appears throughout these studies—namely, the important and often predominant effect on the subject's gastric and colonic function of the relationship existing at the time between the observer and the subject or, in more general terms, the physician and the patient.

Another point I would like to mention is the authors' finding that the colonic changes in anger and hostility were greatest in the two of the four patients who had conspicuous difficulty in expressing their feelings (and these incidentally were the two of the four patients who suffered from ulcerative colitis). This again only confirms what has long been held by psychiatrists, but the demonstration that the actual changes in the colon were greatest in those who appeared to be suppressing their anger is new and impressive.

I believe this study is important not only for its content, but because it represents a new departure—the measurement changes in function in the organs of man, in health and disease, in relation to life situations and emotional states. It may well be the beginning of a new chapter in our understanding of illness.

Health

It seems inescapable that sooner or later we shall come, or indeed we shall be driven by the economic pressure of the cost of sickness, to regard the prevention of disease and promotion of health as more important than the curative or more often palliative medicine to which at present we devote so much more attention. One of the main difficulties seems to be that we have no clear idea of what constitutes health. So far as I can remember, health was not mentioned when I was a student. The mechanismic view of disease which was then the rule left no room for a concept of health, other than in terms of no disease. Just as a machine which was in working order ran, so the body was regarded as healthy so long as there was no breakdown or disease. But good health is something more than no disease, and we can all recognize it when we see it, even though we cannot say just what constitutes it or how to go about getting it. I believe it is our profession's lack of a concept of health, other than as a state of no disease, that leaves the way open for widespread exploitation of the average person's natural desire to enjoy as good health as he can.

My object in raising this question is not to attempt to settle the meaning of health. We are asked to believe, indeed, that this has already been done by the World Health Organization, which has laid it down in most authoritative and uncompromising terms that "health is a state of complete physical, mental, and social well-being; and not merely the absence of disease and infirmity." Here, adds its Director-General, as a kind of warning to meddlesome intruders, is one word concerning the meaning of which the dictionaries will not have to worry from now on (Brock Chisholm, 1949). I need not spend time on this definition (with its necessary implication that all of us are sick, since none of us enjoy complete physical, mental, and social well-being), because it has already been ably examined and criticized by Curran (1952). With all deference to the Director-General of the World Health Organization, I believe we are still far from a satisfactory idea of what constitutes health.

The *Oxford Dictionary* defines health first as "soundness of body; that condition in which its functions are duly discharged," and gives as a further meaning "spiritual, moral, or mental soundness." I imagine it would be generally agreed that health cannot be fully explained in physical terms, and, whatever opinion we hold about disease, health is certainly psychosomatic.

One of the most interesting discussions of health and disease I know of occurs in a small book by Crew (1949) on *Public and Personal Hygiene*. After pointing out that the individual must be capable of adjusting himself to the conditions and circumstances of his external physical and social worlds, he defines health "as that state of the individual in which harmony exists between the various component parts of himself and between the individual as a whole and the circumstances and conditions of his external world."

This definition is a distinct advance, but does not seem entirely satisfactory for at least two reasons: first, no one enjoys complete harmony either in himself or with his external world; and, secondly, health is not so much a state of harmony as the product of a process of continuous adaptation or adjustment, by which a reasonable degree of harmony is maintained. The nearest I can get to an explanation of health—I would not say a definition—is that a person's health depends first on the constitution he is born with, and then on the success he has in constantly adjusting either himself to his environment or his environment to himself, so that a reasonable degree of harmony is maintained both within himself and between himself and the social and material world in which he lives.

But my object in raising this question was not to attempt to settle the meaning of health. It was to point out the need for such a concept, and some of the difficulties in formulating it—difficulties which are, I believe, intimately connected with the questions that I have been discussing. It is no accident that academic medicine has no concept of health; for the mechanismic idea of disease leaves no room for one, other than in terms of no disease, which is clearly inadequate.

Discussion

I would now like to try to pull together some of the apparently disconnected threads of my discursive and eclectic review of some changing concepts in medicine.

Thinking in medicine seems too often to be based on unexamined or insufficiently examined assumptions. It seems often to be taken for granted, for instance, as I have tried to point out, that we can usefully study diseases rather than diseased persons; that all disease or most diseases can be explained in terms of direct mechanical cause and effect; and that diseases can be divided into physical and psychological, with the implication that so-called physical diseases can be studied and treated satisfactorily by exclusively physical methods. In general these individual assumptions add up to a main one, that disease—no one seems to have worried much about health—can be explained in mechanismic or physico-chemical terms.

The rise of so-called psychosomatic medicine, which in America appears already to have assumed very considerable proportions, can best be regarded in a social sense as a revolt against this main assumption; and it is significant that this revolt has coincided with a growing tendency among some physical scientists to question how much their methods can be expected to explain. Strictly, as I have also tried to emphasize, there can be no such thing as psychosomatic medicine or a psychosomatic disease, for these terms involve a confusion between the methods of examination and the objects of study. Health and disease are necessarily psychosomatic, so there cannot be a part of medicine or some diseases which are psychosomatic. What the psychosomatic method does insist—or rather reiterate, for its teachings are as old as medicine—is that in health and disease man must be considered as a whole, and diseased persons must be studied by both physical and psychological methods. It is perfectly true that, in some, much information may be given by physical and little by psychological methods, and in others much by psychological and little by physical methods; but we must not be tempted to conclude from this that there are physical diseases and psychological diseases.

It is often assumed that there is an antithesis of some kind between science and art in medicine. If one were to hazard a guess, a time will come when this too will be regarded as having been a mistaken assumption. When this has happened we shall recognize sciences of pathology, pharmacology, experimental medicine, and so on (for many aspects of disease are explicable in terms of mechanism); and possibly a science of psychology. But strictly clinical medicine will, I believe, be regarded neither as an art nor as a science in itself, but as a special kind of relationship between two persons, a doctor and a patient. It will be recognized that this relationship is the essential feature of clinical medicine; and that the degree of success that it has depends, as in other human affairs, on the skill with which both science and art are called to its aid.

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Australia's greatest pest, the rabbit, is rapidly being brought under control by the planned introduction by the Commonwealth Scientific and Industrial Research Organization of the virus disease myxomatosis. The disease is spread among rabbits by mosquitoes, and in the last three years has gained such ground that the Lands Department of Victoria now estimates that more than 90% of the rabbits have been destroyed in large areas of the State. Similar destruction is reported from many parts of New South Wales, South Australia, and Southern Queensland, with the result that farmers and graziers report a phenomenal increase in the carrying capacity of their pastures. The Minister for External Affairs, Mr. Casey, who is also in charge of the C.S.I.R.O., said that if the gains won at such low cost were maintained Australia's carrying capacity would increase by the equivalent of 10,000,000 sheep. However, he warned that in many districts rabbits were showing an increased resistance to the disease, and that in a very few more seasons myxomatosis might have lost most of its killing power.

THE ANTI-CURARE AGENTS

BY

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It is a truism to say that the only safe remedy for respiratory depression due to curarizing drugs is artificial respiration. It is, however, often very inconvenient to control a patient's breathing until such time as full spontaneous respiratory activity returns. Fortunately there has long been available in "prostigmin" (neostigmine, *B.P.*) an adequate and effective antidote drug. A few years ago, however, several fatalities were recorded shortly after the administration of this agent (Macintosh, 1949; Clutton-Brock, 1949; Hill, 1949). Lately the drug "tensilon" (3-hydroxyphenyl-dimethyl-ethyl ammonium iodide) has been adopted as an anti-curare agent in the United States. It has been investigated in Britain (Doughty and Wylie, 1952; Hunter, 1952) and found to be free from the dangers of excessive parasympathetic stimulation inherent in the action of neostigmine. Unfortunately, tensilon has a very short action, and relapse into partial curarization may occur within some 10 minutes, especially in the deeply curarized subject. Neither antidote is thus completely satisfactory. However, since neostigmine is undoubtedly the more effective of the two, it seemed a matter of some importance to try to elucidate further the dangers of its administration and the methods available for their elimination.

The Investigation

Neostigmine was given to a series of 50 patients who had been curarized with various substitution myoneural blocking agents. All cases had been anaesthetized with nitrous oxide and oxygen and a supplement. It is generally agreed that the primary danger of neostigmine administration is cardiac inhibition. The pulse rates of the patients to whom the drug was given were therefore counted repeatedly at short intervals in order to obtain information on four points: (*a*) the pattern of the response of the pulse rate to neostigmine given with atropine; (*b*) the effect on this of giving the atropine some minutes before; (*c*) the modification induced by giving a sympathomimetic drug with the

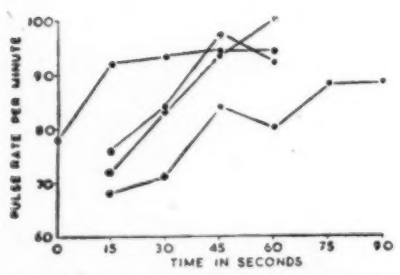

FIG. 1.—Pulse-rate changes after neostigmine, 1 to 1.5 mg., with atropine, 1/100 gr. (0.65 mg.)

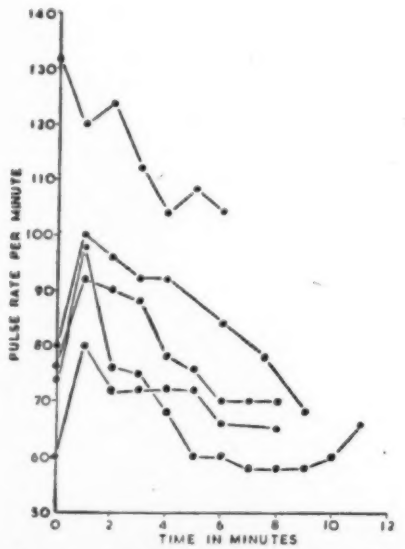

FIG. 2.—Later pulse-rate changes after neostigmine and atropine (doses as in Fig. 1).

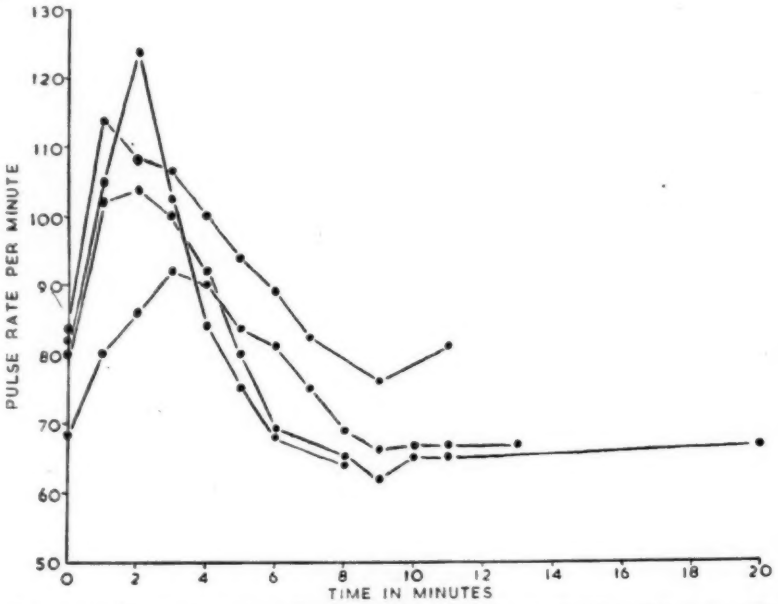

FIG. 3.—Pulse-rate changes after administration of neostigmine, 2.5 mg., with atropine 1/50 gr. (1.3 mg.).

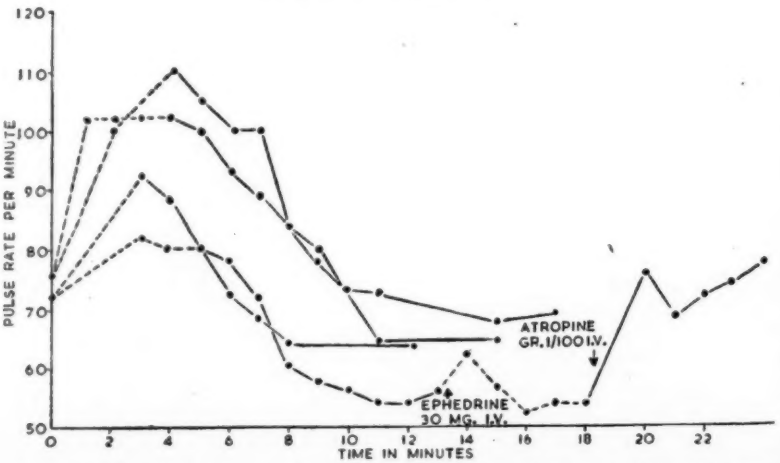

FIG. 4.—Pulse-rate changes after atropine 1/100 gr. (0.65 mg.), followed some minutes later by neostigmine, 1 to 1.5 mg. The time of administration of the neostigmine is indicated by the change from a broken to a solid line in the graph.

atropine and neostigmine; and (*d*) the appropriate amount of atropine required to make the ordinary doses of neostigmine safe.

Pattern of the Response of the Pulse Rate

The obvious danger of the administration of neostigmine is cardiac inhibition. With this in view, the pulse rates of patients to whom this drug was given with atropine were counted every 15 seconds after the injection had been completed (Fig. 1). It will be seen, however, that in every instance such change as did appear was in fact an acceleration and not a slowing. Presently it became apparent that bradycardia developed later in some cases. The pulse rates were therefore counted every minute for as long as possible after the injection of the drugs. In every instance it was found that there occurred a progressive slowing of the pulse rate to a minimum during the first 5 to 10 minutes after the injection had been given. Typical results are shown in Figs. 2 and 3. The slowing in some cases amounted to 60 beats a minute. The ultimate rate attained was related to the initial heart rate. In patients with a tachycardia of 120 or more at the time neostigmine and atropine were given the rate tended to slow to speeds between 70 and 100 a minute. In those whose pulses were relatively slow there was a tendency to obvious bradycardia, and rates of 40 to 50 were sometimes seen.

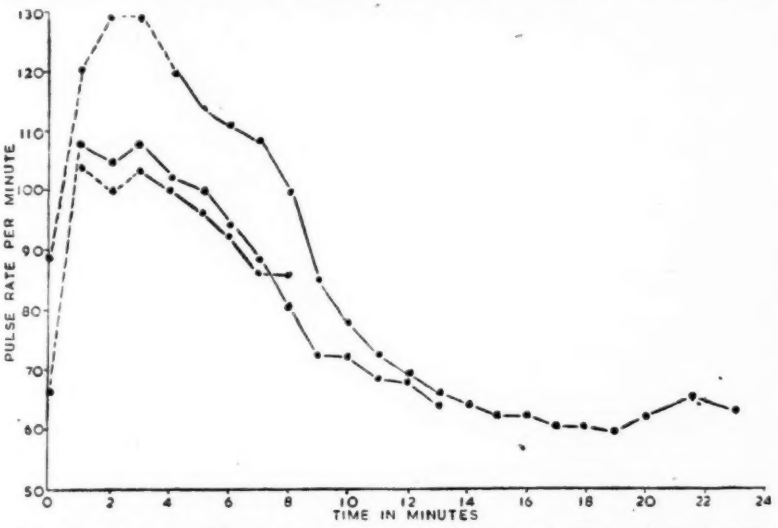

FIG. 5.—Pulse-rate changes after atropine, 1/50 gr. (1.3 mg.), followed some minutes later by neostigmine, 2.5 mg. The time of administration of the neostigmine is indicated by the change from a broken to a solid line in the graph.

Effect of Giving Atropine before Neostigmine

The work reported in the previous paragraph had suggested that in the anaesthetized human subject no initial period of slowing followed the administration of atropine intravenously. None the less, as the view is widely held that atropine slows the pulse by medullary stimulation before its peripheral accelerating mechanism develops, it seemed desirable to obtain direct evidence on this point. The pulse rates were therefore followed in patients to whom atropine was given at varying periods before the neostigmine. Neither with 1/100 gr. (0.65 mg.) (Fig. 4) nor with 1/50 gr. (1.3 mg.) (Fig. 5) was there any evidence of an initial bradycardia. Further, the pulse rate accelerated apparently immediately on the arrival of the drug at the heart. There was no change in the pattern of the response to the subsequently administered neostigmine even in a case in which 19 minutes elapsed between the injection of the two drugs.

Effect of Vasopressor Drugs

In the very early days of curarization in anaesthesia one of my cases became completely pulseless after the injection of neostigmine alone. For some years after that incident it was my habit to inject either 30 mg. of ephedrine or 10–20 mg. of methedrine with the neostigmine and atropine. Patients so treated were investigated in exactly the same way as those already described. It was found that the addition of a vasopressor to the antidote mixture produced a rather greater initial cardio-acceleration (Fig. 6). The pattern of the subsequent slowing of the pulse rate, however, remained unaltered (Fig. 7). There was some suggestion that the minimum pulse rate in these cases was a little higher than those in patients to whom no vasopressor had been given. The differences were

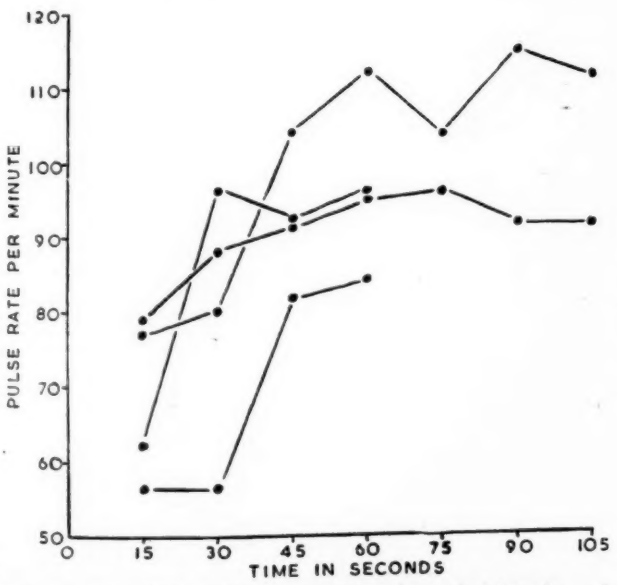

FIG. 6.—Immediate pulse-rate changes after administration of neostigmine, atropine, and a vasopressor drug. Doses: neostigmine, 1 to 1.5 mg.; atropine 1/100 gr. (0.65 mg.); ephedrine 30 mg. or methedrine 10 mg.

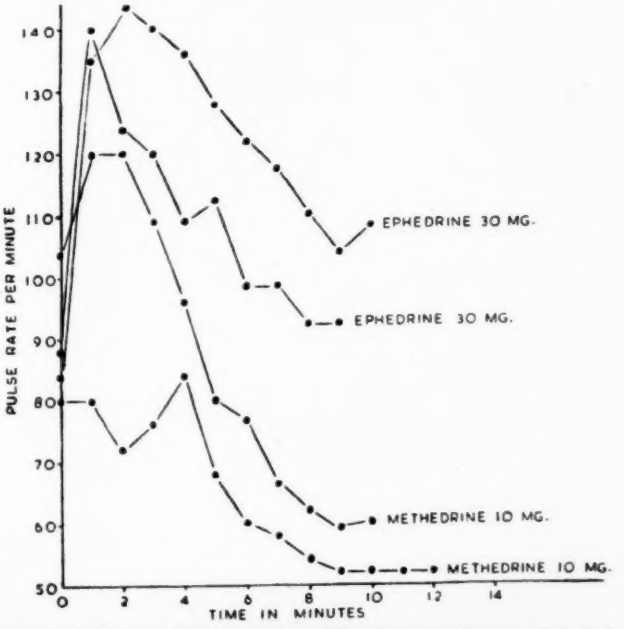

FIG. 7.—Later pulse-rate changes after neostigmine, atropine, and a vasopressor drug. Doses as in Fig. 6.

neither statistically significant nor striking in degree. There therefore seems to be little need for the use of vasopressors with neostigmine and atropine. Further, in two of the patients to whom this combination of drugs was given the pulse became completely irregular two minutes later and then gradually returned through a period of extrasystoles to normal during the succeeding 10 minutes.

Adequate Protective Dose of Atropine

It is very difficult to define a danger point in neostigmine administration, since a pulse rate of 50 may be physiological in a tall trained athlete, yet indicate the presence of a

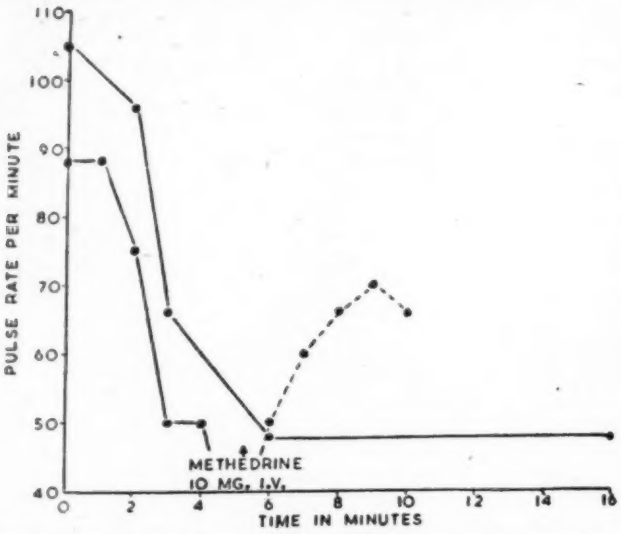

FIG. 8.—Pulse-rate changes after administration of neostigmine, 2.5 mg., with atropine, 1/100 gr. (0.65 mg.)

profound vagal action on the heart in a small untrained woman. None the less, it was assumed for the purpose of this study that a dangerous degree of bradycardia was present when the pulse rate reached 50 a minute after the administration of neostigmine. So far, no patient to whom 1/50 gr. (1.3 mg.) of atropine has been given with neostigmine has developed a bradycardia of less than 50 even with a dose of 2.5 mg. of this drug. Only one of a series of 20 patients to whom 1/100 gr. (0.65 mg.) of atropine has been given with 1 to 1.5 mg. of neostigmine has developed a similar bradycardia. But in the only two patients of this series who received 2.5 mg. of neostigmine with 1/100 gr. (0.65 mg.) of atropine there appeared pulse rates of less than 50 (Fig. 8). In one of these cases methedrine was injected because the interval between the beats became so long that asystole seemed imminent. It is therefore suggested as a tentative working arrangement that 1/50 gr. (1.3 mg.) of atropine should be used when 2.5 mg. of neostigmine is given.

Discussion

The main finding of interest in this study was the absence of an initial slowing of the pulse in the patients to whom atropine was given. It has been believed for years that the first action of this drug is to stimulate the cardio-inhibitor centre in the medulla oblongata. Various studies of different features of its action have demonstrated this, and it has been repeatedly shown that when the drug is injected subcutaneously the first result is beyond question a slowing of the pulse rate (Sturgis *et al.*, 1919, McGuigan, 1921; Harris, 1921; Platz, 1922). This result occurs even with doses of 2 mg. (Bain and Broadbent, 1949). The findings of the present study are not, however, entirely without precedent. There is sound reason to believe that in the human subject, when atropine is rapidly injected intravenously, the initial cardio-inhibitor phase of its action is not in evidence. Thus Platz (1922) found that this was so provided that the dose was greater than 0.5 mg. Smith *et al.* (1928) report that 1.2 mg. of the drug injected intravenously caused a prompt rise in pulse rate. They also comment that slowing sometimes occurred during the injection. If this was so they must have given the drug very slowly, as it requires at least 15 seconds for the transfer of any substance given intravenously at the elbow to the brain, and this interval must have elapsed before the drug they gave could produce any central slowing of the pulse. Shearer (1951), in his study of the action of intravenously injected atropine and scopolamine, found no slowing of the pulse five minutes after the drugs had been given. By contrast, it has become apparent in this study that the maximum effect of neostigmine on the pulse rate is not immediate. It requires at least five minutes for its development. It is thus clear that there is very little danger of summation between the cardio-inhibitor action of neostigmine and atropine injected intravenously in the same syringe.

It is apparent from the degree of bradycardia which has been noted in some of the patients that, even when apparently suitable doses of atropine with neostigmine are given, considerable degrees of cardiac inhibition can still occur. It is thus by no means improbable that the deaths which are reported as having occurred subsequent to the administration of neostigmine were in fact largely due to it. On the other hand, cardiac inhibition due to neostigmine does not occur suddenly and without warning. It is preceded by a gradually increasing bradycardia. If such a phenomenon is observed it is quite safe to inject an additional dose of atropine to accelerate the heart, provided that at least 1/100 gr. (0.65 mg.) is given, and that quickly. There is a corollary to this study. It is impossible to forecast the exact degree of bradycardia which will be produced by a dose of neostigmine. No patient, therefore, to whom this drug has been given should be left unwatched for the succeeding 10 minutes at least.

Summary

The pulse rates of a series of patients to whom neostigmine had been given with atropine, with or without vasopressor drugs, were counted at frequent intervals. It was established that the immediate effect of the intravenous injection of these drugs was a cardio-acceleration. In the subsequent five minutes or so the pulse rate slowed, often a great deal. It may well be that this slowing is an indication that in inadequately atropinized patients cardiac inhibition to the point of standstill may occur.

It is suggested that 1/50 gr. (1.3 mg.) of atropine should be given when 2.5 mg. of neostigmine is used for purposes of decurarization, and even when this amount of atropine is used patients should not be left alone until it has been established that excessive bradycardia is not going to develop—that is, until some 10 minutes has elapsed.

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In the January issue of *Endeavour* (Vol. XII, No. 45) there is an attractive colour plate showing the blotched African genet nursing her kittens. The genet is the only mammal in which cystinuria is known to be a normal condition. Research on the metabolism of the genet now in progress is hoped to reveal new information that will be of value in treating this condition in man.

USE OF INTRAVENOUS ERGOMETRINE TO PREVENT POST-PARTUM HAEMORRHAGE

BY

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"He gently prevails on his patients to try
The magic effects of the ergot of rye."
—TENNYSON.

Sir William Gilliatt (1949) said: "In spite of official statistics, haemorrhage is the most common cause of maternal death. . . . I think it may be said that obstetricians are uneasy in their minds about the management of the third stage and are not satisfied with the method that is usually written and taught." Similarly, Greenhill (1951) asserts that bleeding is the chief cause of maternal death in the United States.

Although the Registrar-General does not publish details of maternal deaths in this country, it is probable that the annual mortality from haemorrhage exceeds 100; Stallworthy (1939) reported it was 365. In Alberta, Canada, during 1936–9 there were 49 deaths due to post-partum haemorrhage in 64,607 deliveries—one death in every 1,318 deliveries (Conn, Vant, and Cantor, 1941). Stabler (1947), writing of the obstetric emergency service in Newcastle-upon-Tyne, states that there were 18 maternal deaths in the 186 flying squad cases of post-partum haemorrhage. In the reports from eight hospitals (Table II) there were 22 deaths associated with haemorrhage in 77,858 hospital deliveries. It would seem a conservative estimate that one in every 5,000 patients delivered in England to-day dies of haemorrhage.

A review of the post-partum haemorrhage rates in University College Hospital over recent years was made from the annual reports, and showed that in the eight years 1942–9, 9% of the total hospital deliveries had a blood loss of 20 oz. (568.2 ml.) (see Table I). There

TABLE I

Year	Total Hospital Deliveries	No. of Cases of Post-partum Haemorrhage*	Blood Transfusion	Manual Removal of Placenta
1949	1,275	104 (8·1%)	12	21
1948	1,210	85 (7%)	20	24
1947	1,233	147 (11·9%)	6	12
1946	1,178	106 (9%)	11	11
1945	1,129	103 (9·1%)	11	10
1944	937	82 (8·9%)	11	7
1943	946	80 (8·5%)	10	17
1942	849	84 (10%)	7	9
	8,757	791 (9%)	88 (1%)	111 (1·3%)

* Measured blood loss of 20 oz. (568·2 ml.) or more.

were two maternal deaths in the post-partum haemorrhage group of 791 cases—one associated with a long labour in a twin pregnancy, and the other showing a phaeochromocytoma at necropsy. The rate for manual removal of the placenta was 1.3% and for blood transfusion 1%.

This high post-partum haemorrhage rate compares unfavourably with that of some hospitals (Table II), but lack of standardization makes comparison difficult. For example, some hospitals take 20 oz. (568.2 ml.) or more as their standard; others take more than 20 oz., more than 600 ml. (21.1 oz.), 500 ml. (17.7 oz.) or more, 1% or more of body weight, etc. (Tritsch and Schneider, 1945; Dieckmann *et al.*, 1947). Theobald (1950) maintains that any bleeding, however slight, which persists after the birth of the child is post-partum haemorrhage. Even more important is the method by which the blood loss is estimated, whether the loss from perineal laceration and episiotomy is included, and the fact that a considerable quantity of liquor amnii may be included, particularly if the uterus fails to contract with the delivery of the baby. Estimates of blood loss based on clinical impression are notoriously inaccurate.

TABLE II

Hospital	Years	No. of Deliveries	No. of Cases of Post-partum Haemorrhage	Blood Transfusion	No. of Manual Removals of Placenta
St. Mary's, Manchester	1943–9	23,125	1,082 (4·7%)	296 (1·3%)	592 (2·6%)
Queen Charlotte's ..	1942–9	17,985	369 (2%)	104 (0·6%)	175 (1%)
United Oxford ..	1942–9	12,543	536 (4·3%)	469 (3·7%)	117 (0·9%)
Elsie Inglis, Edinburgh	1946–9	5,530	281 (5·1%)	62 (1·1%)	119 (2·6%)
British, Woolwich ..	1945–8	5,175	274 (5·2%)	127 (2·5%)	82 (1·6%)
Bromley ..	1946–9	5,105	304 (6·0%)	143 (2·8%)	76 (1·5%)
Guy's ..	1942–9	4,465	353 (8·0%)	Complete details not available	39 (0·9%)
St. Thomas's	1946–50	3,930	552 (14%)	61 (1·6%)	63 (1·6%)
		77,858	3,751 (4·8%)	1,262 (1·7%)	1,263 (1·6%)

Conn, Vant, and Cantor (1941) measured the blood loss in 2,000 normal deliveries: the average loss for primiparae was 388 ml. (13.7 oz.), for multiparae it was 280 ml. (10 oz.), and for the series averaged 323 ml. (11.4 oz.). Dieckmann and Daily (1935) gave the average loss in a spontaneous normal delivery as 107 ml. (3.8 oz.), and in a forceps delivery with episiotomy as 342 ml. (12 oz.). Tritsch and Schneider (1945) reported the mean blood loss noted by 20 different observers as ranging from 100 ml. (3.5 oz.) (Adair) to 600 ml. (21.1 oz.) (Tarnier). It is hardly surprising that these authors list the incidence of post-partum haemorrhage as varying between 0% (Vaux and Mitchell) and 13.7% (Adair *et al.*). Vant (1950), in 2,000 control cases, reported a loss of more than 600 ml. (21.1 oz.) in 15.7%.

The difficulty of comparing reports on post-partum haemorrhage is obvious from these figures, and can be further illustrated by the following figures of University College Obstetric Hospital:

1932–9: 87 cases of post-partum haemorrhage in 8,385 hospital deliveries. A rate of 1%.
1942–9: 791 cases in 8,757 deliveries. A rate of 9%.

This apparent ninefold increase in the haemorrhage rate which occurred since 1942 is not easy to explain, but may be associated with a more careful estimate of the blood loss. We have been unable to incriminate any change of technique at this time, and a similar trend is noticeable in the reports from other hospitals.

Ergot and Prevention of Post-partum Haemorrhage

The use of ergot in the prevention of post-partum haemorrhage is as old as the medical history of the drug.

Dr. Bibley, of New York, writing to Dr. Merriman, says: "In no case where it [ergot] has been used, has haemorrhage occurred, and in natural labour when haemorrhage does occur, it has been given with great advantage" (Merriman, 1820). In 1840 Wardleworth wrote: "As a prophylactic ample experience justifies a reliance on its powers in suppressing haemorrhage. . . . We have repeatedly witnessed its good effects when given to women, some 10 or 20 minutes previous to the delivery." Berry Hart (1912) used intramuscular injection of a liquid extract of ergot as a routine. He wrote: "When the child is born, it is a good plan to give a hypodermic of ergotine into the patient's upper hip. . . . I advise that it should be given in all cases after the head is born, and that one should not wait for haemorrhage before injecting it." But the indiscriminate use of ergot in the second stage has probably done more harm than good, and such abuse has earned it an evil reputation.

Chassar Moir, working at University College Obstetric Hospital, was the first to extract the oxytocic factor from crude ergot and to name it ergometrine (Chassar Moir, 1932; Dudley and Chassar Moir, 1935). Since this description, a number of authors (see Table III) have acclaimed

TABLE III

Author	Dose	Time Given	No. of Cases	Post-partum Haemorrhage Rate	Manual Removal of Placenta Rate
Reich (1939)	0·2 mg. i.v.	With shoulders	154	?4·0%	0·3%
Davis and Boynton (1942)	0·2 mg. i.v.	,, ,,	1,020	0·3% (over 500 ml.)	0·8%
Diddle (1942)	0·2 mg. i.v.	,, ,,	1,960	4·0% (over 500 ml.) 2·1% (over 600 ml.)	0·5%
Roberts (1942)	0·2 mg. i.v.	After birth	400	1·0% (over 500 ml.)	2·5%
O'Connor (1944)	0·2 mg. i.v.	With shoulders	900	0·9%	1·7%
Quigley (1947)	? i.v.	On crowning	430	6·5% (500 ml. and over) 1·0%	1·4%
Léon (1949)	? i.m. (a few i.v.)	With shoulders	639		1·7%
Vant (1950)	0·2 mg. i.v.	,, ,,	4,204	4·3% (over 600 ml.)	?
Lister (1950)	1 mg. i.v.	On crowning	835	0·5% 20+ oz. (568·2 ml.)	1·6%
Daley (1951)	0·5 mg. i.m.	,, ,,	490	9·2% 20 oz. and over (568·2 ml.)	3·5%
Snaith (1951)	0·125 mg. i.v.	Often after birth of baby	187	2·1% 20+ oz. (568·2 ml.)	6·9%

its merits in the prevention of haemorrhage. Many of them are enthusiastic, and the routine use of ergometrine with the birth of the baby would seem to be an increasingly popular procedure in the United States. In England its use is not so widespread. This may be due to its condemnation by Munro Kerr and Chassar Moir (1949), the equivocal findings of Linton Snaith (1951), and the modest claims of Daley (1951). Yet Lister's (1950) results are striking: using 1 mg. of ergometrine intravenously with the crowning of the head in 835 selected cases, she reduced the haemorrhage rate from 16% to 0.4%. Manual removal was neither more frequent nor more difficult, and the injection produced no ill-effects. She concludes that the routine employment of ergometrine in all cases would probably reduce the incidence of post-partum haemorrhage in hospital practice to at least one-tenth of its present level.

Ergometrine (0.5 mg. intramuscularly) was used at University College Obstetric Hospital by Flew (1947) in 500 cases in 1935. There was no constriction ring and no manual removal in this series, but the results were not impressive enough for the routine to be continued.

Some authors (Grimes *et al.*, 1948; Priver *et al.*, 1949) have reported side-effects from using intravenous ergometrine. These include nausea, vomiting, headache, and a slate-coloured cyanosis. We have noticed no such complications.

Present Investigation

At an obstetric staff conference at University College Hospital under the direction of Professor W. C. W. Nixon in April, 1951, it was decided that all cases of vaginal delivery in the hospital should be given intravenous ergometrine (0.5 mg.) with the crowning of the baby's head. The present report deals with the first 1,000 cases so treated, and results are compared with a consecutive series of 1,000 cases taken from the years 1950 and 1951. The comparison is between the conservative and the active treatment of the third stage. All deliveries, except the instrumental ones, were done by medical students under supervision. Blood from vagina and perineum was collected in a kidney dish and measured. Episiotomy under local analgesia was performed if a perineal laceration seemed imminent.

In the "control" group the third stage was conducted in the following manner. Delivery of the baby's shoulders and trunk was not hurried. When the umbilical cord had been cut, the patient's abdomen was uncovered sufficiently for the fundus uteri to be observed. It was not handled.

So long as bleeding was slight the patient was left untouched until signs of separation of the placenta were obvious. Fundal pressure on the contracted uterus was used to assist delivery of the placenta from the vagina. Ergometrine, 0.5 mg., was then given intramuscularly, and bleeding checked by fundal stimulation.

If excessive bleeding occurred before the placenta was delivered or if, after waiting 20 minutes, separation had not taken place, pressure was applied to the contracted fundus uteri and the house-surgeon was called. In the absence of bleeding, preparations for manual removal were started after one hour. The house-surgeon was sometimes allowed to attempt one Credé expression. If there was haemorrhage he gave ergometrine, called the member of the staff on duty, took blood for cross-matching, and prepared for a manual removal.

In the ergometrine series the routine was as follows. Ergometrine, 0.5 mg., was given intravenously by a student with the crowning of the head. The shoulders and body of the baby were delivered slowly. To deliver the placenta a hand was placed on the fundus uteri, which was gently squeezed at the time of the first contraction while traction was applied to the umbilical cord. On completion of the third stage an intramuscular injection of ergometrine, 0.5 mg., was given. If the placenta was retained longer than 15 minutes, or if there was haemorrhage, the house-surgeon was informed.

Results

The control series is made up of 1,090 consecutive vaginal deliveries, of which 101 were forceps deliveries. From this series 36 cases have been excluded for various reasons, chiefly because the data required were incomplete, and three of these had haemorrhages. One of them was a case in which maternal death occurred from haemorrhage following a prolonged labour and forceps delivery. A further 54 cases were excluded because ergometrine was given with the birth of the baby, and all were forceps deliveries. In the remaining 1,000 cases the results were:

Primary post-partum haemorrhage (blood loss of 20 oz. (568.2 ml.) or more) ..	131 cases (13.1%)
Secondary post-partum haemorrhage (excessive loss in the puerperium)	3 cases (0.3%)
Manual removal of the placenta	11 cases (1.1%)
Blood transfusion	18 cases (1.8%)

Comparative figures in the ergometrine series were:

Primary post-partum haemorrhage	12 cases (1.2%)
Secondary post-partum haemorrhage ..	8 cases (0.8%)
Manual removal of placenta	30 cases (3.0%)
Blood transfusion	5 cases (0.5%)

This series consists of the first 1,000 cases given ergometrine intravenously, and comes from a group of 1,221

consecutive vaginal deliveries. In 176 (14.4%) ergometrine was not given either because the student failed to get the needle into the vein as the head crowned or because he was not present at delivery. (This failure rate was reduced to 10% in the last 500 cases.) In 42 patients the ergometrine was given intramuscularly, and in three cases the required data were not available. There were 19 primary haemorrhages and 1 secondary haemorrhage in the 221 excluded cases, and this figure includes two concealed accidental haemorrhages in which most of the post-partum loss was clot formed before birth.

A comparison of the blood loss in the two groups is seen in Table IV. The difference in the mean blood loss of the two groups is significant at the 1% level, and the conservation of blood in the ergometrine group is considerable.

TABLE IV

Amount of Blood Loss	% In Control Series		% In Ergometrine Series	
0–9 oz. (0–255·7 ml.)	64		89·2	
10–19 ,, (284·1–539·8 ml.)	22·9		9·6	
20–29 oz. (568·2–823·9 ml.)	7·8	13·1	0·7	1·2
30–39 ,, (852·3–1,108 ml.)	3·0		0·3	
40–49 ,, (1,136·4–1,392·1 ml.)	1·4		0·2	
50 oz. (1,420·5 ml.) and over	0·9		—	

Post-partum Haemorrhage

The haemorrhage rate of 13.1% in the control series is higher than stated in the annual report of the hospital because deliveries by caesarean section are excluded and all losses of 20 oz. (568.2 ml.) are included.

The time of administration of pethidine and the weight of the baby were studied in the 131 post-partum haemorrhages and the findings compared with 131 random cases. It could not be shown that pethidine administration increased the haemorrhage rate as Barnes (1947) showed in her report from this hospital. Large babies—over 9 lb. (4.1 kg.)—were significantly more frequent, as Reich (1939) reported. Any tendency towards heavy bleeding in forceps deliveries was due to loss from lacerations, although inexpertly administered or prolonged anaesthesia is a well-recognized cause of increased blood loss.

Delayed haemorrhage some hours after delivery (as reported by Lister, 1950) was not a feature of our treated series.

Secondary post-partum haemorrhage occurred in three cases in the control group and in eight in the ergometrine group. All three in the control group and four in the ergometrine group had a retained placental cotyledon. In the remaining four only fragments of placental tissue and decidua were removed at curettage.

Manual Removal

There were 41 cases of manual removal of the placenta in the 2,000 cases—30 in the ergometrine series, and 11 in the control group. The indication for the operation is seen in Table V.

TABLE V

	Manual Removal	
	For Retained Placenta	For Post-partum Haemorrhage
Ergometrine series	23	7
Control series	2	9

In the present series placental retention is increased (statistically significant at the 1% level) by the use of intravenous ergometrine. Out of the group of 23 cases in Table V there were five in which the injection of the ergometrine was given too late, and one breech delivery. In each of these cases the uterus did not contain the foetal body when it contracted—a situation which predisposes to placental retention. It has been a recent practice of some operators to remove the placenta manually after a forceps delivery if it does not show immediate signs of separation, and this accounts for a further 6 of the 23 cases. The operation performed under such circumstances in a fit patient is safe, and, in our opinion, is not made more difficult by the use of ergometrine. In two cases in the ergometrine series the placenta was incompletely removed, resulting in a primary and a secondary haemorrhage, both avoidable.

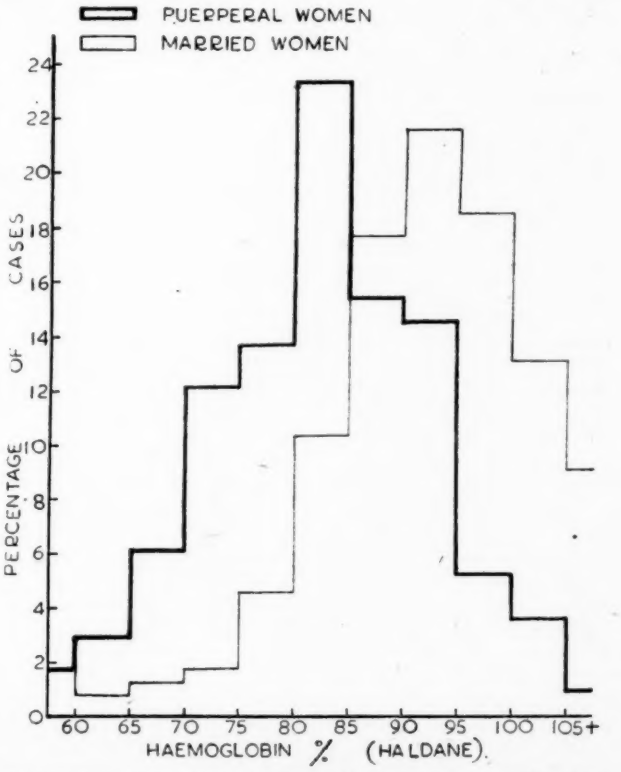
Haemoglobin Level and Blood Loss

A haemoglobin estimation by Haldane's method is done on all patients on the fourth or fifth day of the puerperium. The results in the 2,000 cases are given in Table VI.

TABLE VI

Haemoglobin	% In Control Group	% In Ergometrine Group
Below 60%	2·5	1
60–64%	3·6	2·4
65–69%	6·7	5·6
70–74%	12·7	11·7
75–79%	13·8	13·7
80–84%	24	22·7
85–89%	13·1	17·7
90–94%	13·9	15·2
95–99%	4·4	6·1
100–104%	3·9	3·3
105% and above	1·4	0·6

The standard deviations of the two groups are significantly different at the 1% level. The means of the two groups are not significantly different, but blood loss may occur without affecting the haemoglobin level; for the latter is dependent on haemodilution, which occurs in some cases and not in others (Dyson, Plaut, and Vaughan, 1943). The mean haemoglobin in the control group is 82%, and in the ergometrine group 83.4%. This difference, though small, is probably due to the greater blood loss in the first group, as there is a tendency for large blood loss to be associated with a low haemoglobin. This can be seen from the fact



Post-partum haemoglobin in the 2,000 cases of the series compared with that reported by the Medical Research Council (1945) in married women.

that 37.4% of those who lost more than 20 oz. (568.2 ml.) had haemoglobin values below 70% (49 out of 131), while only 9.1% of the remainder were below this value (79 out of 869). Among the ergometrine group those with a haemoglobin under 70% were 58.3% (7 out of 12) of patients with blood loss greater than 20 oz. (568.2 ml.) and 8.5% of the remainder (84 out of 988).

In the Chart the post-partum haemoglobin in the 2,000 cases is compared with that reported by the Medical Research Council (1945) in married women in this country. The numbers have been combined for this purpose, since the difference between the two sets of 1,000 is small compared with the difference between married and puerperal women. This report also stated that in the last trimester of pregnancy 9% of women had haemoglobin values under 70, and 37% had values under 80. The corresponding figures in our post-partum series are 12.8% and 39.3% in the control group, and 9% and 34.4% in the ergometrine group.

Length of Third Stage of Labour

There is no doubt that ergometrine reduces the length of the third stage, as Table VII shows. In the ergometrine series it was less than 20 minutes in 94% of cases.

Davis and Boynton (1942) noted that there was a direct relationship between blood loss and length of the third stage —an observation which is confirmed in our treated cases.

TABLE VII

Length of Third Stage	% In Control Group	% In Ergometrine Group
0–4 minutes	1·5	50·3
5–9 ,, ...	9·0	33·6
10–19 ,, ...	51·5	10·4
20–29 ,, ...	28·0	1·1
30–39 ,, ...	6·4	1·2
40+ ,, ...	3·6	3·4

Discussion

Intravenous ergometrine, if given with the crowning of the foetal head, causes a striking reduction in blood loss in the third stage of labour and a marked lowering of the post-partum haemorrhage rate. It also shortens the length of the third stage. These facts seem indisputable. Those authors who are not wholly in favour of using ergometrine, such as Roberts (1942) and Snaith (1951), admit that the timing of the injection was not accurately made, or else, like Daley (1951), they gave the ergometrine intramuscularly. We consider timing a most important point: intravenous ergometrine acts within a minute of injection, causing a tonic uterine contraction and placental separation while part of the baby still occupies the uterine cavity. Placental expression should be carried out as soon after the birth of the baby as possible. To facilitate this, cord traction is a useful and safe procedure. In a firmly contracted uterus the only danger of cord traction is the theoretical risk of causing acute inversion of the uterus, but, as Picton (1951) points out, before inversion can be initiated uterus and cervix must be relaxed.

In our series there was an increased incidence of manual removal of the placenta when ergometrine was used (3% as compared with 1.1% in the control series). The higher rate of this complication is used by some as an argument against intravenous ergometrine therapy. As we have pointed out, there is a tendency in this hospital towards a more frequent use of this procedure, particularly after instrumental deliveries. Recognition of the value of cord traction would possibly result in fewer manual removals, as might digital exploration of the upper vagina described by Graber (1950), revealing a placenta trapped in the cervix and therefore easily removed without anaesthesia. Smellie (1754) recommended both pulling on the cord and digital exploration to feel the placenta.

It would be wrong to claim that post-partum haemorrhage is eliminated by using ergometrine. The drug has no effect on bleeding from cervical or vaginal lacerations. Occasionally the uterus fails to contract after 0.5 mg. of intravenous ergometrine, and there are other factors which may cause bleeding, such as an abnormal coagulation mechanism (Reid, 1951).

There is the disadvantage that an assistant must be available to give the injection at the right moment. In hospital this should not be too difficult to arrange. In domiciliary practice it is far less easy. This is a strong argument for teaching midwives the technique of intravenous injection.

We conclude by advocating a more widespread use of this technique, in the belief that it would prevent much puerperal morbidity and some maternal deaths.

Summary

Intravenous ergometrine, 0.5 mg., was given to 1,000 patients in the second stage of labour with the crowning of the foetal head. The results are compared with 1,000 control cases.

The use of ergometrine has shown: (1) A reduction in the primary post-partum haemorrhage rate from 13.1% to 1.2%. This is significant at the 0.1% level. (2) A reduction in the amount of post-partum anaemia. (3) A shortening of the third stage of labour. (4) A significant increase in the rate of manual removal of the placenta from 1.1% to 3%.

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HAEMOGLOBIN LEVELS IN A GROUP OF ELDERLY PERSONS LIVING AT HOME ALONE OR WITH SPOUSE

BY

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Wintrobe (1951a) stated, "there are few satisfactory data for the blood in old age." Some studies of haemoglobin levels—for example, by Olbrich (1947) and Howell (1950)—have been carried out on old persons living in hospitals or institutions or under especially favourable conditions. Relatively little similar work, however, appears to have been done on adequate numbers of old people living under natural conditions in their own homes. A medical survey of old persons living alone or with spouse in Sheffield enabled us to carry out such a study.

Methods

1. Selection of Group.—The sample drawn in March, 1948, was a 1:30 random selection from the food office register in Sheffield of men and women who had reached pensionable age (65 in men and 60 in women). Only those living alone or with spouse were included in the medical survey. The haematological investigations were not carried out until at least one year later. Those eligible for inclusion were interviewed by a social worker, who invited their co-operation. Subjects who were willing were then medically examined in their homes and samples of blood were taken. The final group consisted of 177 men between the ages of 66 and 85, and 246 women between the ages of 61 and 87.

2. Dietary Survey.—Information was collected on the food and drink consumption of each subject for a period of one week. A spring balance and standard tablespoons and teaspoons were provided (Widdowson, 1936; Beltram and Bransby, 1950). During the dietary survey the subject was visited three or four times by a field worker to ensure that the records were being properly kept. From these records the average daily intake of the various nutrient principles was calculated. The dietary survey was satisfactorily completed by 56% of the group.

3. Samples of Blood.—To a suitable quantity of dry ammonium and potassium oxalate (Heller and Paul, 1934) 5 ml. of venous blood was added, the whole being gently agitated. From the blood sample the following investigations were carried out.

(*a*) *Haemoglobin Levels.*—Between September, 1949, and May, 1950, these were determined by the Haldane method (Whitby and Britton, 1950a), using N.P.L. calibrated pipettes and comparator (100% Hb=14.7 g./100 ml.). Over the next and last 12 months the determinations were made in an M.R.C. photometer (King *et al.*, 1948), using oxyhaemoglobin (100% Hb= 14.8 g./100 ml.). Approximately the same number of haemoglobin determinations were made by each of the two methods. The variances of the determinations made by the Haldane method and of those made in the M.R.C. photometer were 2.22 and 2.10 respectively. As there was no significant difference between the variances of results obtained by the two methods, all the determinations were pooled to facilitate analysis.

(*b*) *Red cells* were counted by a standard method in an improved Neubauer counting chamber (Wintrobe, 1951b).

(*c*) *Absolute values* (P.C.V., M.C.V., M.C.H.C.) were determined by the Wintrobe (1951c) method in those samples showing less than 11.7 g./100 ml. of haemoglobin.

(*d*) *Blood smears* were stained by the Leishman method (Whitby and Britton, 1950b).

4. Emphysema.—A diagnosis of pulmonary emphysema was made on the appearance of chest *x*-ray films by Dr. J. L. A. Grout, consultant radiologist—182 females and 138 males whose haemoglobin had been estimated were examined radiologically.

Results

Haemoglobin in Relation to Age and Sex.—The mean haemoglobin levels of the 177 males and of the 246 females were calculated, giving values of 14.4 g./100 ml. for the males and 13.8 g./100 ml. for the females. Using the large sample method (Fisher, 1941) for testing the significance of the difference between two means, the standard error of the difference was calculated (0.16), and the difference (0.6) was found to be significant. Thus the females had a signifi-

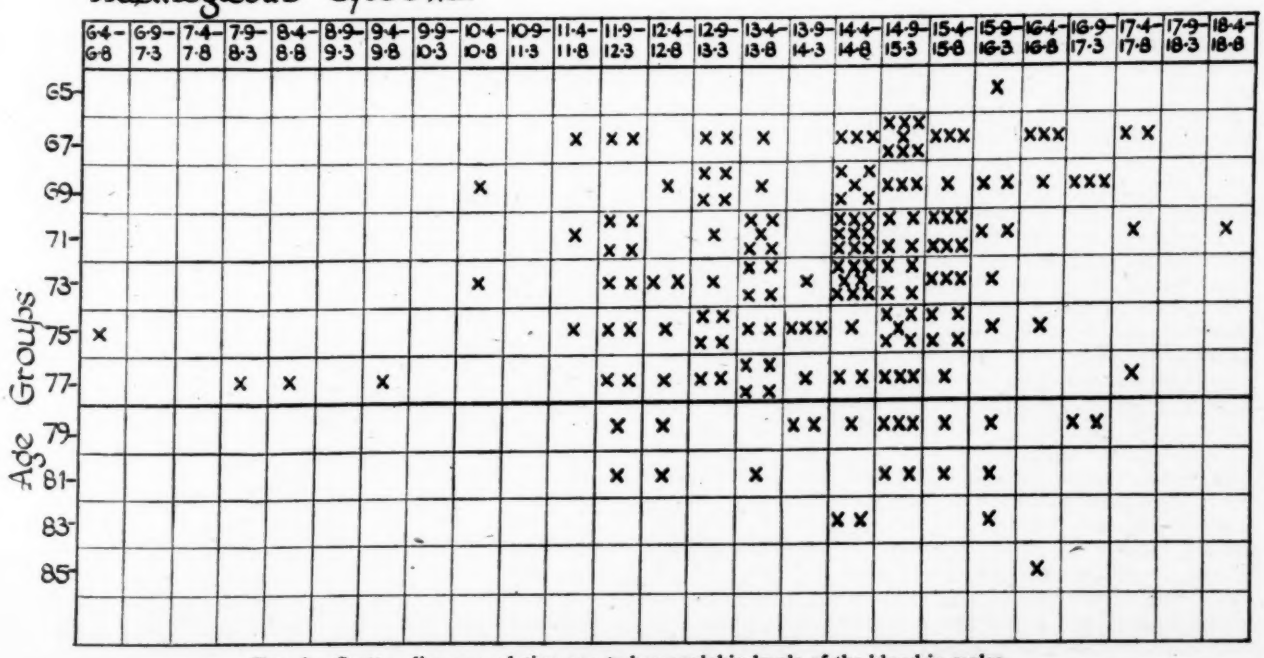

FIG. 1.—Scatter diagram relating age to haemoglobin levels of the blood in males.

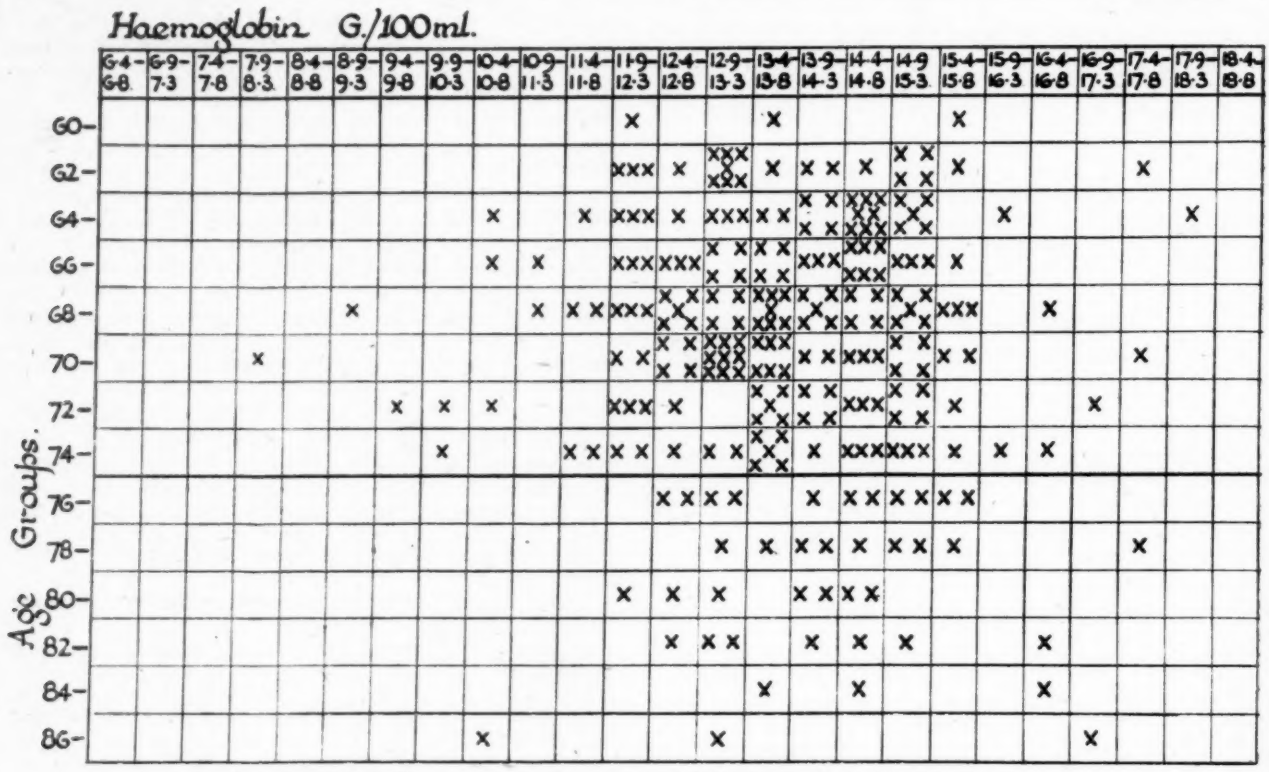

FIG. 2.—Scatter diagram relating age to haemoglobin levels of the blood in females.

cantly lower haemoglobin level than the males. The relationship between haemoglobin content of the blood and age is shown in the scatter diagrams (Figs. 1 and 2). Although from these diagrams there does not appear to be an overall correlation between haemoglobin levels and age, a negative correlation over the age range 65.5–77.5 years for the males and over the age range 60.5–74.5 years for the females is apparent.

The correlation coefficient between haemoglobin level and age for the males within the age range 65.5–75.5 years was calculated and found to be significant ($r=-0.2799$, $n=154$, $P < 5\%$), whilst the correlation coefficient over the complete age range was not significant ($r=0.1077$, $n=177$, $P > 5\%$). Similarly for the females, the correlation coefficient over the age range 60.5–74.5 years was significant ($r=-0.262$, $n=204$, $P < 5\%$), whilst that over the complete range was not significant ($r=0.068$, $n=244$, $P > 5\%$). Thus over a certain age range there was a significant decrease in the haemoglobin content of the blood with increasing age in both sexes, but beyond this age range the haemoglobin levels were narrowly scattered round the mean level for each respective sex group.

Haemoglobin and Social Class.—Based on the classification of occupational status of the Registrar-General, the subjects were divided into three groups: professional and managerial (Class I and II of the R.-G.), skilled workers (Class III of the R.-G.), and semi-skilled and unskilled workers (Class IV and V of the R.-G.). There was no significant difference between the haemoglobin levels in either men or women in the different occupational groups.

Haemoglobin Levels in Those Living Alone compared with Those Living with Spouse.—The mean haemoglobin level of the 46 males living alone was 13.9 g./100 ml. compared with a mean level of 14.5 g./100 ml. in the 131 males who were living with their wives. This difference was significant at the 5% level of probability ($t=2.06$). There was no significant difference between the mean haemoglobin levels of the females who lived alone (13.9 g./100 ml.) and those who were living with their husbands (13.8 g./100 ml.). Thus living alone seems to be aetiologically significant for the males but not for the females.

Haemoglobin Level and Emphysema.—It is often taught that patients with emphysema show a high haemoglobin content of the blood. The mean haemoglobin level of the 45 females showing radiological evidence of emphysema was found to be lower than the mean level in 137 females showing no emphysema. The mean haemoglobin level of the 32 males with radiological evidence of emphysema was slightly higher than that of 106 males showing no emphysema. These differences were not significant. Hence this study does not lend any support to the thesis that in old people with emphysema there is a high haemoglobin content of the blood.

Causes of Anaemia in this Group

Any person with a haemoglobin level of 11.7 g./100 ml. (80% Haldane) or less was arbitrarily considered to have anaemia. Absolute values were estimated in these cases. The incidence of anaemia was as follows: men, 9 cases (5.1%); women, 16 cases (6.5%). It was possible to obtain dietary figures for only the more co-operative cases with anaemia—namely, five men and eight women.

In addition, information on the social and clinical condition of the subjects was available. Eight out of the nine male cases had microcytic anaemia of the iron-deficiency type. The other had macrocytic anaemia associated with Paget's disease. Three out of the 16 female cases suffered from macrocytic anaemia; the rest had microcytic anaemia of iron-deficiency type.

Under the conditions of our survey it was not possible to carry out other investigations—for example, fractional test meals.

In at least 11 out of the 25 cases of anaemia a poor diet seems to have been a contributory factor. Apathy and a low income were the chief reasons for inadequate diets. On the other hand, at least four cases appeared to have had adequate diets.

Another contributory factor was rheumatoid arthritis in seven cases, particularly in women (six cases). Chronic haemorrhage was not detected clinically in any case.

Syphilis in one woman, scurvy in another, and chronic alcoholism in one man were the only other recognizable potential contributory conditions.

Discussion

As different methods have been used for haemoglobin determinations, and as varying standards have been set from time to time for the 100% level, using the same technique, comparison of our results with those of previous workers is feasible only if the results are expressed in grammes per 100 ml. The figures obtained in this survey of old people living in their own homes (14.4 g./100 ml. for males and 13.8 g./100 ml. for females) are in close agreement with those found by Olbrich (1947) for people living in institutions (13.9 g./100 ml. for males and 13.2 g./100 ml. for females).

Howell (1950) obtained very high values (18.3 g./100 ml. for men and 16.6 g./100 ml. for women) in a group of elderly patients in a hospital for the chronic sick. On the basis of these results he was unable to agree with statements made by earlier workers that "old people are anaemic." Exclusion of cases of anaemia and malignant disease, a higher standard of diet than in many cases found in our survey, and use of the Sahli method on the ward may all have played a part in determining his high results.

So far as we are aware, all observers agree that the level is higher in men than in women for all age groups. The present study confirms this observation so far as the elderly are concerned. The Committee on Haemoglobin Surveys (1945) found that in men the mean level tends to fall in later life; the information provided in our study confirms this view. They found, however, that the haemoglobin level in women falls slightly between the ages of 30 and 49, but rises again after that; this fall and rise may be associated with the occurrence and cessation of menstruation respectively. It would appear, however, that in women over 60 the cessation of menstruation no longer plays a part in causing a rise in haemoglobin. The fall in haemoglobin with age in both sexes may be partly due to decreasing ability to absorb haemopoietic substances. Thus Polland (1933) has shown that the incidence of achlorhydria increases with age. The decrease may also be due to diminished intake of iron, since our survey showed that the intake of iron diminished in both sexes with age. The cessation of these trends in extreme old age is a phenomenon which we have found in other physiological estimations—for example, serum cholesterol, blood pressure. If a relatively low haemoglobin content of the blood gives a diminished risk of survival there may well be a selective removal of those with low haemoglobin levels, particularly in extreme old age, when the death rate is very high. In these circumstances the mean levels in these older age groups would tend to be higher. It would appear that the mean haemoglobin level falls with age in both sexes until extreme old age; this fall is interrupted in women by the cessation of menstruation, but ultimately resumes the downward trend.

The studies of Monroe (1951) on 7,941 patients over the age of 61 in a geriatric hospital revealed a much higher incidence of anaemia than in the present survey. He found that 15.5% of the men and 11.2% of the women had a haemoglobin level of below 70%. We are unable to make a strict comparison with our figures, as the method of haemoglobin estimation was not given. Monroe stated: "Loss of blood was the commonest cause of severe secondary anaemia in old age (522 cases). Malignant disease was the source of the blood loss in over half of them, closely followed by peptic ulcer and cirrhosis of the liver. Infection caused anaemia in 165 cases. Usually it was mild, but those due to the streptococcus occasionally produced so rapid a fall in blood counts as to suggest blood loss." Hence the idea that old people are anaemic may have arisen from hospital experience. These causes are very different from those found in the present study.

One of the most interesting findings of the survey was the lower haemoglobin level of the males living alone compared with those living with their wives.

The cases of anaemia in this group of elderly people living in their own homes were largely due to adverse social factors, such as apathy, a low income, or, in the case of males, living alone. A meals-on-wheels service would have helped considerably.

Anaemia seems to be a condition which is very easily missed in old people, as none of our cases were receiving any form of treatment for it. A simple haemoglobin estimation in all old people would be of great value for detecting a potentially remediable cause of ill-health.

Summary

The haemoglobin levels of 177 men between the ages of 66 and 85 years and of 246 women between the ages of 61 and 87 years were determined. All these old people were living in their own homes either alone or with spouse. In men and women there was a significant downward trend over a certain age range, and the males (mean haemoglobin level 14.4 g./100 ml.) had a significantly higher level than the females (mean haemoglobin level 13.8 g./100 ml.).

There was no significant social class difference in haemoglobin levels in either males or females.

Pulmonary emphysema was not associated with a high haemoglobin content of the blood.

Males living alone had significantly lower haemoglobin levels than those living with their wives. There was no difference in the case of females.

Nine men (5.1%) and 16 women (6.5%) had haemoglobin levels of 11.7 g./100 ml. or less. Eight of the men and 13 of the women had iron-deficiency anaemia, while one man and three women had macrocytic anaemia. None of the patients were having any form of treatment for their anaemia. The main contributory factors appeared to be poor diet (44%) and rheumatoid arthritis (28%). Apathy and a low income were the chief reasons for the poor diet. A simple haemoglobin estimation in all old people would be of considerable value for detecting a potentially remediable cause of ill-health. A meals-on-wheels service would have been of benefit.

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CLINICAL TRIAL OF PHENYLINDANEDIONE AS AN ANTICOAGULANT

BY

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At present dicoumarol and ethyl biscoumacetate (*bis*-3, 3'-(4-oxycoumarinyl)-ethyl acetate; "tromexan") are the two drugs with a prothrombopenic action which are in common use as anticoagulants. Dicoumarol was the first prothrombopenic drug to come into use, but its toxic effect (due, however, in many instances to indiscriminate heavy overdosage and also to lack of proper control, including unreliable estimations of the prothrombin time) has led to severe haemorrhage in many cases. The great drawback with dicoumarol is its cumulative action, which may continue long after the drug has been stopped. This cumulative effect necessitates particularly skilled and detailed control of the drug with frequent estimations of the prothrombin time if severe haemorrhage is to be avoided. Another disadvantage with dicoumarol is the long delay, usually 48 to 72 hours, before a full therapeutic effect is reached.

Ethyl biscoumacetate has a much more rapid action than dicoumarol, a therapeutic effect usually being achieved in 18 to 24 hours. Moreover, the effect of ethyl biscoumacetate, unlike that of dicoumarol, is, owing to the rapid metabolism and elimination of the drug, almost never cumulative. The rapid inactivation of ethyl biscoumacetate, however, often makes it difficult to maintain an even therapeutic prothrombin concentration, especially in the initial stages of treatment. In addition, the wide individual variation in the reaction to ethyl biscoumacetate is another factor requiring detailed and meticulous control in every case.

In recent years a new prothrombopenic drug, phenylindanedione, has aroused interest and been the subject of clinical trial. In 1944 Kabat, Stohlman, and Smith showed that certain indanedione derivatives have a specific action in reducing the plasma prothrombin. Soulier and Gueguen (1947) reported satisfactory results from using phenylindanedione, the most active of the indanedione derivatives. Jaques *et al.* (1949) found no toxic effects from phenylindanedione in animals. Blaustein *et al.* (1950) reported their observations on the use of the drug in 53 patients, and concluded that phenylindanedione had an action similar to but more rapid than that of dicoumarol. Bjerkelund (1950) found that phenylindanedione had not only a more rapid effect but also a more uniform action than dicoumarol. In addition, Bjerkelund showed that phenylindanedione had no effect on factor V.

The present paper is a report on the use of phenylindanedione in 68 patients. Most of them were suffering from coronary thrombosis or deep venous thrombosis, and in several there was evidence of cardiac failure. Quick's one-stage method was used for estimation of the prothrombin time, and the thromboplastin was a phenol–saline emulsion prepared from human brain. Therapeutic prothrombin levels of 10–20% (or approximately twice to three times the normal prothrombin time) were aimed at.

Rapidity of Action and Recovery

In practically all cases 200 mg. of phenylindanedione (divided into two equal doses) was given in the first 24 hours, followed by 100 mg. (in two equal doses) in the next 24 hours. On this dosage only 6 cases out of the 68 failed to reach an adequate therapeutic prothrombin level in 48 hours, whilst in only one of these was the prothrombin level above 40% at this time. In many cases in which the prothrombin time was estimated at 36 hours it was found that an adequate therapeutic level had been attained by this time. In most of the 68 cases an appreciable lowering of the prothrombin concentration to 50% or below was reached by 24 hours.

The effective action of phenylindanedione passes off fairly rapidly, and therefore the risk of cumulative effects is slight except where very large doses are given. Twenty-four hours after stopping the drug there was either no change or only a small fall in the prothrombin times in those patients in whom the prothrombin had previously been maintained at a full therapeutic level (10–20%) for at least several days. Up to 36 hours after cessation of phenylindanedione there was still an appreciable effect, but between 36 and 48 hours after the last dose there was a sudden sharp drop in the prothrombin time to near normal levels. By 72 hours the prothrombin times in practically all cases had become normal or almost so.

The return to normal of the prothrombin time in patients on phenylindanedione depends (as with other similar anticoagulants) largely on the level to which the prothrombin had been depressed. The lower the prothrombin concentration, the longer it takes for a normal prothrombin content to be regained. Again, any lowering of renal function will delay the excretion of the drug. In the very few cases in which the prothrombin time failed to return to normal or near normal within 48 to 72 hours after the last dose there were signs of deficient renal function.

The absorption and recovery rates of phenylindanedione are therefore midway between those of dicoumarol and ethyl biscoumacetate. Phenylindanedione has many advantages over dicoumarol in its quicker effect and the very slight danger of cumulative action. On the other hand, although it is not as rapid in action as ethyl biscoumacetate its more prolonged effect makes it much easier to maintain a therapeutic prothrombin level over a prolonged period. Ethyl biscoumacetate is practically all metabolized and excreted within 24 hours, so that omission of the drug for only one day will result in even an excessively prolonged prothrombin time returning to normal or near normal and the drug therefore losing its therapeutic effect. This rapid inactivation, combined with the wide individual variation in the reaction to the drug, necessitates the most detailed and experienced control when ethyl biscoumacetate is used. With phenylindanedione, however, the time-lag of 36 hours before there is any really appreciable change in the prothrombin concentration allows ample time for the clinician to ascertain the prothrombin level and to readjust the dose of phenylindanedione when necessary without wide fluctuations in the prothrombin level occurring.

Dosage

The initial dosage in all 68 cases was 200 mg. (100 mg. morning and evening) the first day, followed by 100 mg. on the second day. By 48 hours the full effect of this dosage was evident, and, according to the prothrombin level then reached, it was possible to estimate with a fair degree of accuracy the further doses needed for maintenance therapy. The greater the rise in the prothrombin time by 36 to 48 hours the more sensitive the patient is to the drug and the smaller the daily maintenance dose that is required. In 44 of the 68 cases this daily maintenance dose lay between 75 and 100 mg. and in only 5 cases did it fall outside the range of 50–150 mg. (see Table). The variation

Maintenance Doses of Phenylindanedione

No. of Cases	Daily Maintenance Doses in mg.	No. of Cases	Daily Maintenance Doses in mg.
2	50	3	125
4	50–75	2	125–150
22	75	4	150
4	75–100	2	150–175
18	100	1	175
4	100–125	2	175–200

in individual susceptibility to phenylindanedione is therefore not very great and seems to be much less than with either dicoumarol or ethyl biscoumacetate.

In all cases the total daily dose of phenylindanedione was given in approximately two equal amounts morning and evening. Dividing up the total daily dose seems to give more uniform results.

Guides to Dosage

There are several factors which help greatly in estimating the required maintenance doses in individual cases. Before, however, these are considered it is necessary to stress one important point. The initial doses for the first two days should (subject to the exceptional cases mentioned below) invariably be kept constant. To give a *larger* dose than 100 mg. on the second day, solely on the result of one prothrombin estimation taken 24 hours or less after starting treatment, will lead in most cases to too high a dose being given. The *full* effect of phenylindanedione is not evident for 36 to 48 hours.

To give a *smaller* dose than 100 mg. on the second day may, however, be justifiable where the prothrombin time at 24 hours (if taken) is already within a therapeutic range. In these few cases the dose of phenylindanedione on the second day may be reduced from 100 to 75 mg.

With phenylindanedione, as with all anticoagulants of the coumarin group, the extent of individual susceptibility is most important, so that the ultimate control of therapy in all cases lies in frequent prothrombin estimations. There are, however, several factors which can help in gauging, with some accuracy, the required maintenance doses of phenylindanedione:

1. Weight is important; the heavier the patient the more likely it is that the daily maintenance doses will be on the large size—that is, 125–175 mg.

2. The more acutely ill the patient (especially cases of coronary thrombosis accompanied by severe shock) the smaller the maintenance doses of phenylindanedione that are needed. It was noticed in several cases, however, that the maintenance doses in the acutely ill patients had to be increased later on when there was an improvement in their clinical condition.

3. Age is not so important in itself, but as older people tend to be more frail they require smaller doses. The apparent age is more important than the real age.

4. Renal function is of particular importance in gauging phenylindanedione (as other anticoagulant) therapy. Deficient renal function will lead to delayed excretion of the drug, so that much smaller maintenance doses are necessary. In this series the few cases in which there was an unexpectedly sharp rise in the prothrombin time were those in which it was not realized that renal function was depressed. As the majority of patients with lowered renal function are in the older age groups, it has been found most useful to perform routine blood-urea estimations in all patients of 60 and over.

Taking all the above factors into account, it will be found that the less acutely ill robust young patients require the largest maintenance doses of phenylindanedione, whilst the seriously ill frail elderly patients need the smallest doses.

Toxic Effects

No toxic effects were noticed in this series of 68 cases and there was no case of haemorrhage. Soulier and Gueguen (1947) reported dryness in the mouth, polydipsia, polyuria, and tachycardia with phenylindanedione, but in their cases very large doses, in the neighbourhood of 700 mg. and over, were given. In a small series of seven cases of mine in which large doses of phenylindanedione were given in order to produce a severe prothrombin deficiency far in excess of that required for therapeutic purposes, no toxic effects were noticed apart from haematuria in one case only. In most patients on phenylindanedione the urine turns a pinkish-orange colour; this is of no significance.

Antidote.—The great drawback in anticoagulant therapy with drugs of the coumarin group has up till recently been the lack of a really effective antidote. Water-soluble vitamin-K analogues have only a very limited effect in correcting a severe prothrombin deficiency. Vitamin K_1, however, even by mouth, has a most dramatic and rapid effect (within 8 to 20 hours in most cases) in overcoming the prothrombopenic action of dicoumarol, ethyl biscoumacetate, and phenylindanedione (Toohey, 1952).

Frequency of Prothrombin Estimations

After the initial two or three prothrombin estimations necessary in the first four to five days of therapy, it is usually sufficient to carry out prothrombin estimations only twice or, at the most, three times a week. Phenylindanedione is very stable in its action, so that once the individual variation in reaction has been assessed it is not necessary to do daily prothrombin estimations.

It is perhaps advisable to point out here that minor unimportant fluctuations in the prothrombin time, as measured by the one-stage method, are often seen in practice in patients on anticoagulants. Therefore, to avoid unnecessarily frequent alterations in the maintenance doses of phenylindanedione and similar anticoagulants, the method of prothrombin estimation used should allow for a comparatively wide margin in the clotting-time within which the therapeutic control may be regarded as satisfactory. For this reason, phenol–saline thromboplastin is particularly suitable in that the effective therapeutic range of the prothrombin time is two to three times the normal control (or 30 to 45 seconds).

The administration of heparin interferes with the estimation of the prothrombin clotting-times. Therefore, if the patient is having heparin as well as phenylindanedione the sample of blood for prothrombin estimation should be taken at least four hours, and preferably six hours, after the last dose of intravenous heparin.

Summary and Conclusions

Phenylindanedione has been tried as an anticoagulant in 68 patients, mostly cases of coronary thrombosis and deep venous thrombosis. It is a very effective anticoagulant which in its action lies approximately midway between dicoumarol and ethyl biscoumacetate. The dangerous cumulative effect of dicoumarol occurs to a far lesser extent with phenylindanedione, whilst the fact that the metabolism and excretion of phenylindanedione is less rapid than that of ethyl biscoumacetate makes clinical control of anticoagulant therapy with phenylindanedione much easier.

In this series of 68 cases 200 mg. (in two equal divided doses) was given on the first day, followed by 100 mg. on the second day. On this dosage an appreciable fall in the prothrombin level was noticed in 24 hours, and a full therapeutic effect, with a prothrombin concentration in the region of 10–20%, was reached in 36 to 48 hours in nearly all cases.

The further daily maintenance doses of phenylindanedione varied between 50 and 200 mg. In 44 of the 68 cases the maintenance dose lay within the limited range of 75 to 100 mg., and in only five cases did it fall outside the range of 50–150 mg. Phenylindanedione seems to be much more uniform in action, and therefore easier to control, than either dicoumarol or ethyl biscoumacetate.

Important factors in assessing the appropriate daily maintenance dose within the range of 50 to 175 mg. are the weight, age (apparent rather than real), general health, and renal function. The more robust, young, and less acutely ill patients require the largest doses, whilst the frail, elderly, and severely ill cases need the smallest maintenance doses. Any lowering of renal function will materially reduce the amount of phenylindanedione required.

Once the daily maintenance dose has been established, this dose can be continued for a prolonged period without any significant fluctuation in the prothrombin times. (With improvement in a severely ill patient's general condition, a small increase in the daily maintenance dose may sometimes be necessary.) This uniform action of phenylindanedione means that in most cases, once the daily maintenance dose has been established, prothrombin estimations are necessary only twice or, at the most, three times a week. (In patients on prolonged therapy, prothrombin estimations weekly or less often are usually enough.)

No toxic effects from phenylindanedione were encountered in this series. In a small series of seven cases reported previously, the giving of much larger doses than those required to maintain an adequate therapeutic prothrombin level resulted in haemorrhage in one case only and no other toxic reactions. This haemorrhage and the severe prothrombin deficiency seen in the other six cases were quickly controlled within eight to twenty hours by vitamin K_1 given orally.

The total daily dose of phenylindanedione in each case was given in two divided amounts, morning and evening. In most cases it turns the urine a pinkish-orange colour.

I wish to thank Charles E. Frosst and Co. (Canada) for the initial supplies of phenylindanedione ("danilone") and also Evans Medical Supplies Ltd. for additional amounts of the drug ("dindevan"). I also wish to express my gratitude to Dr. E. Lozinski, of Charles E. Frosst and Co., for his help and advice.

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Robert James Graves, who died on March 20, 1853, is best remembered to-day for his accurate account of exophthalmic goitre (1835). Although earlier descriptions of the condition were given by Flajani (1802) and Parry (1815), it is best known in Britain as "Graves's disease." He was one of the founders of the Park Street School of Medicine in Dublin. While physician to the Meath Hospital he introduced Continental methods of clinical teaching with good effect. Graves qualified in 1818 and then studied in London and on the Continent. When he was in Austria his fluency in languages led him to be taken for a German spy and he was imprisoned for ten days. During a journey from Genoa to Sicily the ship in which he was travelling ran into a storm and the crew threatened to abandon ship. Graves seized an axe and smashed the ship's boat; he then assumed command and repaired the pumps with leather from his own boots. Graves contributed many papers to medical literature. His *Clinical Lectures on the Practice of Medicine*, 1848, is considered his best work.

TREATMENT OF NAUSEA AND VOMITING OF PREGNANCY WITH ANTIHISTAMINES

BY

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During the past few years good results have been reported from the use of antihistamine preparations in nausea and vomiting of pregnancy. Dougray (1949) recorded 94 cases thus treated, with 83% cured, and Carliner *et al.* (1949) reported on 43 patients treated with dimenhydrinate ("dramamine"), with 72% cured. At St. Andrew's Hospital during the past three years a large proportion of patients complaining of nausea and vomiting in pregnancy were freed from these symptoms by taking an antihistamine preparation. So successful was this treatment that it was extended to patients who complained mainly of heartburn, with equally gratifying results. After some months it was decided to make a clinical trial, treating one group of patients with an active antihistamine preparation and another group with an inert preparation.

Method

Although all patients were questioned as a routine on vomiting in pregnancy, only those who specifically complained were treated. Cases were divided into three groups: severe vomiting, in which vomiting occurred at frequent intervals during the day or caused the patient a good deal of distress; occasional vomiting, in which vomiting was not frequent and regular and did not unduly distress the patient; and cases in which heartburn and nausea were the predominant symptoms. No attempt at clinical assessment was made, apart from excluding any obvious non-obstetric cause of vomiting, and the patient's own statement was the guide to the group in which she was placed. As the element of suggestion plays a part in the treatment of these patients, and some patients will respond to any form of therapy, it was decided to include only those who had already received some other form of treatment without improving.

Two antihistamine preparations were used, both in tablet form: mepyramine maleate ("anthisan"), 100 mg., and promethazine-8-chlorotheophyllinate ("avomine"), 25 mg. They appeared to be equally effective. The control tablets contained lactose only, and were identical in size and shape, and almost identical in colour with the active tablets. Patients were divided into two groups of 60; one group was treated with antihistamine tablets and the other group with the inert tablets. The tablets were collected from the hospital dispensary and enough for three days' treatment were given. Patients were instructed to take a tablet at night before retiring. This routine was altered occasionally for those whose symptoms were particularly troublesome at a set time—for example, after the evening meal or after getting into bed at night. These patients were instructed to take the tablet about two hours before the expected time of onset of the symptoms.

Patients were seen five days later at the antenatal clinic. Those who were free from symptoms while taking the tablets were classified as cured; others were classified as improved or unchanged. The short period of three days for treatment was chosen because experience had shown that patients who were going to benefit by the treatment did so almost immediately. There was also the additional factor that by giving a short course of treatment and by

seeing the patients soon afterwards there was less risk of their forgetting the facts or becoming confused about details.

Results

Of the 60 patients who were treated with an active antihistamine preparation, 47 reported themselves as cured and six as improved. Thus 88% were either cured or improved by the treatment. In the control group, three patients regarded themselves as cured and four as improved, a total of 10%. Table I shows that no case of severe vomiting

TABLE I.—*Results of Treatment*

Treatment	No. of Cases	No. Cured	No. Improved	No Change
	Severe Vomiting			
Antihistamine ..	31	25	2	4
Inert tablet ..	33	—	—	33
	Moderate Vomiting			
Antihistamine ..	17	12	3	2
Inert tablet ..	16	2	4	10
	Nausea and Heartburn			
Antihistamine ..	12	10	1	1
Inert tablet ..	11	1	—	10

was affected by an inert preparation, and that it was in the cases of moderate vomiting that the inert tablets had most effect.

Most of the patients in the control series were subsequently treated with antihistamines, when they showed a higher proportion of cured and improved (Table II). Thus

TABLE II.—*Control Cases Subsequently Treated with Antihistamines*

No. of Cases	No. Cured	No. Improved	No Change
50	43	3	4

out of 50 of these patients treated 86% were cured, 6% were improved, and only 8% showed no change. With this group, however, other factors may have affected the results. These patients were being treated at a somewhat later stage in pregnancy, and it was possible that time was effecting a cure. Also, as the antihistamine tablets they subsequently received were of a brighter colour than the inert tablets, they may well have deduced that they were receiving a more potent preparation, and so the factor of suggestion may have influenced the results.

In most cases three days' treatment was insufficient to effect a permanent cure, and it was necessary to continue treatment for at least a fortnight, and sometimes for four weeks. No other treatment was given and no dietary restrictions were imposed. No adverse effects were noted from even a prolonged course, although occasionally some patients complained of drowsiness.

Comment

The causes of nausea and vomiting in pregnancy are not known, and it is therefore a matter of speculation why the antihistamines give relief. Finch (1938) suggested that nausea and vomiting of pregnancy are due to an allergic tendency, and that the patient had become sensitized to some secretion of her own corpus luteum. He carried out intradermal tests with corpus luteum extract and found that the reaction produced was in direct proportion to the degree of nausea and vomiting present. Kapeller-Adler and Adler (1943) have shown that there is an increased histamine production by the body in pregnancy. They suggest that, whereas in normal pregnancies the serum is able to inactivate histamine, in cases of hyperemesis gravidarum and mild pre-eclampsia the serum has lost this power and in consequence there is an excess of histamine in the body, and it is this excess which is responsible for the disturbed gastric function.

These theories offer some explanation for the mode of action of the antihistamines. On the other hand, it is well recognized that most of the drugs used for their antihistamine properties have some depressant action on the central nervous system, and it is possible that they exert their influence by lowering the sensitivity of the vomiting centre.

Some of the patients who did not respond to treatment improved after the dosage was increased or when a more powerful form of antihistamine such as promethazine hydrochloride, 25 mg. twice daily, was given. This confirms Dougray's experience, although he found it necessary to give a higher dosage.

A number of patients had a recurrence of symptoms in the latter weeks of pregnancy, and these were all successfully treated with antihistamines. It is occasionally taught that vomiting late in pregnancy is of serious significance, but in the absence of any evidence of pre-eclampsia this is not so.

Summary

A number of patients suffering from gastric disturbances in pregnancy were treated with antihistamine preparations and an equal number were given an inert preparation. The results showed that a high proportion of patients obtained relief with the antihistamines and only a small proportion were relieved with the inert preparation.

My thanks are due to Messrs. May and Baker for a generous supply of avomine tablets and for supplying the inert tablets.

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ACUTE NITROBENZENE POISONING WITH TRANSIENT AMINO-ACIDURIA

BY

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AND

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Many cases of nitrobenzene poisoning have been recorded. The majority of these have been due to accidental ingestion, contact, or inhalation, especially in industry. The case reported here was the result of a deliberate attempt at suicide and showed the usual characteristic manifestations of methaemoglobinaemia. There was also a marked transient amino-aciduria.

Case Report

A married woman aged 24, living apart from her husband and 4-year-old son, became depressed and decided to commit suicide. At 11 a.m. she swallowed "about half a bottle" of a bee mixture, which was clearly labelled as a poison. So far as could be ascertained later, she drank about 1 oz. (28 ml.) of this mixture, which contains nitrobenzene (or oil of mirbane) 2 parts, safrol oil 1 part, and petrol 2 parts. Therefore she may have swallowed almost 200 minims (12 ml.) of nitrobenzene.

She found the taste of the mixture most unpleasant and noted a burning sensation in her mouth. Half an hour

later she vomited twice and felt dizzy and had to be helped to her bed. After a further half-hour she was seen to be deeply cyanosed. Her relatives became alarmed, and with some difficulty persuaded her to go to hospital. She was admitted in the early afternoon of December 13, 1951.

On admission she was hysterical and strongly resented having her stomach washed out with sodium bicarbonate. Her breath and the odour of the gastric residue were suggestive of floor polish. There was an intense blue-grey cyanosis, especially of the lips and face and beneath the finger-nails. She soon became more rational, although apprehensive, and told us that she had swallowed the bee mixture in an attempt to end her life. This preparation is popular with bee-keepers, and we had no difficulty in discovering that nitrobenzene was the active ingredient.

Examination revealed that the pulse was of poor volume but regular at 120 beats a minute. Her blood pressure was 120/70. There was no gross peripheral circulatory failure. She was given 1/30 gr. (2 mg.) of strychnine sulphate by hypodermic injection. An intravenous drip was begun soon after admission. Normal saline was given at first, but when we concluded that the cyanosis was due to methaemoglobinaemia, 2 ml. of 10% methylene blue was injected into the drip tubing. Immediately afterwards the intravenous saline was replaced by blood and the patient was placed in an oxygen tent. There was no immediate change in colour, but approximately 20 minutes after the injection of methylene blue her colour reverted to normal. In view of this and as she was not obviously anaemic, the blood transfusion was discontinued after 350 ml. of blood had been given. For the next 24 hours 5% glucose by slow intravenous drip was given. Ascorbic acid, 1 g., was added to each pint (570 ml.). Two hours after admission the pulse rate was 88 and the blood pressure 110/70. The respirations had been rapid on admission, but soon became normal as the patient became more composed. A sample of blood which had been taken as the intravenous drip was started revealed methaemoglobin spectroscopically. A specimen of urine obtained later did not contain albumin or sugar.

The following day the blue-grey cyanosis was again intense and the patient complained of a severe headache, dizziness, and a bad taste in her mouth. The urine contained methaemoglobin and methylene blue in large amounts. Intravenous therapy was abandoned and the following oral regime begun: 16 gr. (1 g.) of methylene blue a day in divided doses and 200 mg. of ascorbic acid thrice daily.

On December 15 the intense cyanosis remained but she felt fairly well. The next day she complained of nausea and low back pain. On December 17 blood examination showed: haemoglobin, 85% (Haldane), or 12.6 g. per 100 ml.; red cells, 4,220,000; white cells, 6,650 (neutrophils 42%, eosinophils 3%, lymphocytes 45%, monocytes 10%). There was no punctate basophilia. The patient remained cyanosed but was free from symptoms.

On December 18 urinary chromatography, using the "rack tank" technique of Datta, Dent, and Harris (1950), revealed alanine, glutamine, serine, glycine, taurine, tyrosine, glutamic acid, and β-amino*iso*butyric acid, all present in concentrations markedly in excess of the normal. Two days later the cyanosis finally disappeared and the patient felt well, but on December 24 she became dizzy when she was out of bed. Blood examination revealed: haemoglobin, 66% (Haldane), or 9.7 g. per 100 ml.; red cells, 2,860,000; colour index, 1.12; white cells, 12,750 (metamyelocytes 4%, neutrophils 54%, eosinophlis 6%, lymphocytes 34%, monocytes 2%); corrected E.S.R., zero; P.C.V., 28%; M.C.V., 98 μ^3; M.C.H.C., 34%. A blood film showed polychromasia and anisocytosis with slight macrocytosis.

On December 27 the patient complained of nausea, but her appetite was good. Haemoglobin was 63% (Haldane), or 9.3 g. per 100 ml.; red cells, 2,890,000; colour index, 1.07; corrected E.S.R., zero; P.C.V., 30%; M.C.V., 103 μ^3; M.C.H.C., 31%; white cells, 11,050 (neutrophils 58%, eosinophils 8%, lymphocytes 32%, monocytes 2%). On January 5, 1952, the haemoglobin was 65% (Haldane), or 9.6 g. per 100 ml.; red cells, 3,260,000; colour index, 0.98; corrected E.S.R., zero; P.C.V., 31%; M.C.V., 94 μ^3; M.C.H.C., 32%; white cells, 7,900. Although the blood picture was slowly reverting to normal the patient was given 2 pints (1,140 ml.) of blood by intravenous drip, to expedite recovery.

Blood examination on January 12 showed: haemoglobin, 85% (Haldane), or 12.6 g. per 100 ml.; red cells, 3,950,000; colour index, 1.06; corrected E.S.R., 7 mm. in one hour; P.C.V., 38%; M.C.V., 94 μ^3; M.C.H.C., 33%; white cells, 9,200; reticulocytes, 2.5%. On January 12, and again on February 8, the urinary chromatogram was normal.

The patient remained afebrile throughout her stay in hospital and was never jaundiced.

Discussion

This case differs from cases of nitrobenzene poisoning reported by Chapman and Fox (1945) and Nabarro (1948) in that cyanosis was noted one hour after the ingestion of the nitrobenzene, which was much sooner than in their cases. The odour of nitrobenzene is quite distinctive and has been likened to that of essence of bitter almonds by Nabarro.

Hamblin and Mangelsdorff (1938) found methaemoglobin in the blood of all cases of nitrobenzene poisoning, whereas Loeb, Bock, and Fitz (1921) were unable to detect it and suggested the formation of a nitrobenzene haemoglobin compound. In our case the spectrum for methaemoglobin was obtained, although with considerable difficulty, in spite of the intense degree of cyanosis. Nabarro (1948) suggested that if methylene blue was given transfusion might not be necessary, and our case confirmed this, as the blood picture was definitely improving spontaneously before the second blood transfusion. It is unfortunate that the effect of methylene blue seems to be transient. Its mode of action has been discussed fully by Gibson (1948).

In view of the results obtained by Deeny, Murdock, and Rogan (1943) in the treatment of congenital methaemoglobinaemia with ascorbic acid we gave the patient large doses of this vitamin, although Shils and Goldwater (1949) concluded that the beneficial effect of ascorbic acid in experimental and human benzene poisoning was not convincing.

Wirtschafter and Wolpaw (1944) have recorded a case of nitrobenzene poisoning in which there was a low total plasma protein content, a decrease in cholesterol esters, and slight but significant bromsulphthalein retention. It is probable that in their case, as in ours, there was an acute zonal hepatic necrosis. The condition must have been quite transient in our case, as subsequent urinary chromatography and extensive liver and kidney function tests did not reveal any abnormality. Uzman and Denny-Brown (1948) reported persistent amino-aciduria in early cases of hepato-lenticular degeneration (Wilson's disease) before liver-function tests showed any abnormality, and this has been confirmed in a similar case in this hospital. Himsworth (1950) considered that urinary chromatography was the best means of demonstrating amino-acids in the urine in cases of acute liver atrophy, and he suggested that their presence in this condition signified not only that liver cells had been killed but that few survived.

Wirtschafter and Wolpaw recommended glucose to fortify the liver and saline to replace that lost by vomiting. They dismissed replacement blood transfusion as unnecessary, but thought that the inhalation of oxygen in high concentration helped to prevent the formation of methaemoglobin, and they concluded that nitrobenzene affects the circulatory, respiratory, and central nervous systems both directly by toxic action and indirectly by the formation of methaemoglobin, with resultant anoxaemia. They thought that the hepatic and haemopoietic systems were damaged by direct toxic action.

Summary

A case of acute nitrobenzene poisoning is recorded in which there was methaemoglobinaemia and amino-aciduria. Urinary chromatography revealed a transient gross excess of all the normal amino-acids. The literature on the symptomatology and treatment of the condition is reviewed briefly. The patient made a rapid recovery.

For permission to publish this case we are indebted to Dr. Robert Marshall and to Dr. J. A. Smyth, physician-in-charge, Biochemistry Department. We wish to thank Dr. M. G. Nelson for the haematological reports, and Mr. J. S. Coulter, F.I.M.L.T., for the spectroscopic demonstration of methaemoglobin.

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ACUTE TETRACHLORETHANE POISONING

A REPORT ON TWO FATAL CASES

BY

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Cases of acute tetrachlorethane poisoning, following its ingestion by mouth, are unusual. Only three such cases are reported in the English literature (Hepple, 1927; Elliott, 1933; Forbes, 1943). Acute tetrachlorethane poisoning is generally suicidal, its distinctive odour rendering its accidental ingestion unlikely. One case of acute accidental poisoning has, however, been recorded (Hauser, 1939). There is no record of tetrachlorethane having been used as a homicidal agent.

Tetrachlorethane is a colourless, non-inflammable, oily liquid, boiling at 146.3° C., and with a specific gravity of 1600 at 20° C. It is soluble in fats, oils, resins, and waxes, miscible with alcohol, and soluble in water to the extent of 1 part in 5,000. It has a sweetish smell and taste, somewhat resembling trichlorethylene, carbon tetrachloride, and chloroform, but quite distinct to those who are familiar with it. The commercial preparations have a yellow tinge. As a solvent, tetrachlorethane has many applications in industry, but, owing to its intensely poisonous properties, being the most toxic of the halogenated hydrocarbons (Hamilton, 1934; Browning, 1937), it is falling into disuse. At one time it was issued to the Army as "silk cleansing fluid," and two of the three acute cases recorded in the English literature occurred in soldiers. Its widest application outside industry is in horticulture—as an effective insecticide against white fly. In the two cases described below, the tetrachlorethane was originally purchased as an insecticide.

Chronic tetrachlorethane poisoning has been described and reviewed by a number of authors (Willcox, 1915; Minot and Smith, 1921; Legge, 1934; van Oettingen, 1937; Forbes, 1943). Methods for the early detection of chronic tetrachlorethane poisoning by examination of the blood and urine have been described by Minot and Smith (1921), and Gurney (1943). Toxic jaundice due to tetrachlorethane poisoning became compulsorily notifiable in this country after January 1, 1916, as the result of cases occurring amongst aircraft workers, who used it as "dope" for the treatment of fuselage. Twenty-six cases, five of which were fatal, were notified in 1916, but no further cases were notified until a fatal case occurred in 1929. Although chronic tetrachlorethane poisoning is becoming virtually unknown in this country, cases are still occurring abroad. Seven such cases, one of which was fatal, have been recorded by Coyer (1944).

When taken in large quantities by mouth, tetrachlorethane kills by its narcotic action before recognizable changes can take place in the liver and other organs. Consciousness is rapidly lost, and this is followed by a gradual depression of the vital centres, death occurring some 10 to 20 hours after ingestion. In these cases, except for the presence and smell of tetrachlorethane, the necropsy findings are those of narcotic poisoning, with changes in the gastric mucosa depending on the quantity taken and the presence or otherwise of food. In the two cases to be described the tetrachlorethane had been deliberately taken by mouth.

Case 1

A gardener aged 57 had become depressed because the estate on which he had been employed for thirty years was about to change hands. He left home one day as usual at 7 a.m., taking his sandwiches with him. As his mother, with whom he lived, was often in bed before he returned home in the evening, he was not missed until the next morning. At about 10 a.m. on that day he was found dead on the floor of his potting-shed; an uncorked bottle of tetrachlorethane lay by his side and a short farewell note was found scrawled in chalk across his work-bench.

Necropsy was carried out the next morning. A strong smell of tetrachlorethane was apparent on entering the mortuary. The body was that of a well-nourished man. There was an intense cyanosis of the post-mortem livid stains. Anoxic haemorrhages were present in the scalp.

There was no corrosion of the mouth, lips, or tongue. The lower third of the oesophagus was congested, and early superficial necrosis of the mucosa was present. At the cardiac end of the stomach extreme congestion of the entire gastric mucosa was found, with superficial necrosis and frank erosion. At the pyloric end of the stomach the exposed ridges of the rugae were principally affected. From the stomach and the first half of the duodenum 15 oz. (425 ml.) of tetrachlorethane was recovered. The tetrachlorethane had not passed beyond this point. The stomach also contained a further 5 oz. (142 ml.) of fluid consisting mainly of mucus. Food was not present.

Numerous anoxic haemorrhages were scattered throughout the brain, and there was early basal collapse of both lungs. No material natural disease was present in other organs.

Case 2

A carpenter aged 20, recently discharged from the R.A.F., was depressed over an error he had made at work. On the day before his death he returned home as usual for lunch. He had a good meal and left the house at 1.20 p.m. to return to work. At 2.30 p.m. it was noticed that his bicycle was still in the garden, and almost immediately afterwards he was found unconscious in a wheel-barrow which was standing close to a greenhouse. Later a medicine bottle which contained tetrachlorethane was found in the greenhouse, with approximately 1 to 2 oz. (28 to 57 ml.) missing.

He was admitted to hospital at 4.15 p.m., where he was found to be unconscious; his limbs were flaccid and all reflexes were absent. His pupils were contracted and unreactive. He was cyanosed. His pulse was good and the blood pressure was 140/90. There was a sweet smell in his breath which was thought to be due to trichlorethylene. He was given oxygen and admitted to a ward, where his stomach was washed out with water. Three and a half litres of stomach washings were retained. During the wash-out he vomited the whole time, but was prevented from inhaling the vomit by tipping. The wash-out was stopped as his breathing was becoming weaker. Eventually breathing stopped completely. An intratracheal tube was passed, and artificial respiration was carried out with Boyle's apparatus. His heart then stopped beating, but recommenced after an injection of nikethamide. Breathing began naturally after two injections of 12 mg. of picrotoxin, but the respiratory excursion remained very poor in spite of two further injections that day. His condition deteriorated during the night and his heart again stopped, but started spontaneously. Later his breathing stopped and picrotoxin had no further effect. Death occurred at 5.30 a.m. the following day—about fifteen hours after he had ingested the poison.

Necropsy was carried out on the same day. A distinct smell of tetrachlorethane was present at the lips. A fine froth was found in the mouth and issuing from between the lips. There was an intense cyanosis of the post-mortem livid stains.

The brain was oedematous and congested, and a number of small anoxic haemorrhages were scattered throughout the white matter. Both pleural cavities contained a small clear exudate. The air passages were filled with copious frothy oedema fluid, and the lower lobes of both lungs were virtually airless as a result of extreme congestion and oedema. There was a small clear pericardial effusion. Numerous anoxic petechial haemorrhages were present on the epicardial and endocardial surfaces of the heart, and were most noticeable on the interventricular septum. No natural disease of the cardiovascular system was found.

There was no corrosion of the mouth or throat. The lower end of the oesophagus was congested. The stomach contained 440 ml. of fluid, consisting of water, mucus, a little undigested food, and free tetrachlorethane. Pronounced congestion of the gastric mucosa was present, affecting principally the ridges of the rugae. There was no necrosis, and the gross appearances resembled nicotine poisoning. A small blood-tinged peritoneal exudate was present, and congestion of the duodenum and upper jejunum. The other organs were normal, as was the histology of the liver and kidneys.

Free tetrachlorethane was recovered from the alimentary tract as follows:—Stomach: total contents, 440 ml.; free tetrachlorethane, 23 ml. Duodenum: total contents, 115 ml.; free tetrachlorethane, 21.5 ml. Small intestine (jejunum and upper ileum): total contents, 550 ml.; free tetrachlorethane, 4 ml. There was no free tetrachlorethane in the 3,500 ml. of stomach washings retained by the hospital.

Discussion

Acute and chronic tetrachlorethane poisoning are two distinct entities. In the latter, tetrachlorethane acts on the liver, heart, kidneys, and haemopoietic system, differing from the other halogenated hydrocarbons only by its higher toxicity, death resulting from liver necrosis a few weeks after the onset of symptoms. In its acute form of poisoning tetrachlorethane behaves as a narcotic, death usually occurring some 10 to 20 hours after its ingestion. Consciousness, however, seems to be lost early. The interval between ingestion and death, and the appearances of the gastric mucosa, depend on the quantity taken and the presence or otherwise of food in the stomach. In Case 1 it would seem that death occurred with extreme rapidity after the ingestion of a very large volume of tetrachlorethane taken on an empty stomach. In Case 2 a much smaller quantity of tetrachlorethane was taken immediately after a large meal, and, although consciousness appeared to have been rapidly lost, death did not occur for some 15 to 16 hours. Vigorous resuscitative measures undoubtedly prolonged life in this case. It is quite clear from Case 2 that, owing to the insolubility of tetrachlorethane in water and its very high specific gravity, it is unlikely to be satisfactorily evacuated from the stomach by the normal methods of lavage.

Summary

Two cases of acute fatal tetrachlorethane poisoning have been described. The differences between acute and chronic tetrachlorethane poisoning are discussed.

Ordinary methods of gastric lavage are unlikely to be satisfactory.

I wish to thank H.M. coroner, West Surrey, for permission to publish these two cases.

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ANAL FISTULA WITH EXTENSION TO THE THIGH

BY

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A case of chronic ulcerative colitis is presented in which a fistula extended from the anal canal through the space between the sacro-spinous and the sacro-tuberous ligaments and then along the obturator internus tendon to form an abscess in the thigh.

Case Report

A man now aged 37 first complained of diarrhoea and the passage of blood and mucus per rectum in 1938. In 1939, following a haemorrhoidectomy and excision of a fistula-in-ano, the diarrhoea increased in severity, and he also began to pass pus per rectum. In 1940 signs and symptoms of an anal stricture developed, and for its relief a caecostomy was performed. Later that year he also developed a vesico-colic fistula, and his weight fell to 6 stone (38.1 kg.). A transverse colostomy was then constructed and the caecostomy closed by operation. Since 1940 the transverse colostomy had acted many times a day; and during that time he had complained of pain in the region of the right hip.

On April 26, 1949, he was first seen by me at Sydney Hospital. He stated that he had had more severe pain over the right hip for the previous three months, and for six months had noticed a swelling over the right greater trochanter.

On examination his general condition was fairly satisfactory, his weight was 9 stone (57.2 kg.), and his height 5 ft. 7 in. (170 cm.). The abdomen was lax and not tender,

and no mass or viscus was palpable. There were operation scars in the right iliac fossa. The transverse colostomy in the epigastrium was retracted to the level of the surrounding skin, which was indurated.

A sigmoidoscope with an external diameter of 1 cm. passed easily into the proximal limb of the colostomy and revealed slightly reddened mucosa, but no blood, mucus, or pus was seen. The mucosa was not ulcerated and there was no constriction of this portion of the bowel. The same sigmoidoscope passed only 8 cm. down the distal loop of the colostomy. Further passage was prevented by a stricture with a lumen of only a few millimetres. The mucosa of this portion of the bowel was covered with blood, pus, and mucus, but no ulceration was present. While air was being blown into this distal limb of the colostomy the patient complained of pain and a feeling of bubbling in the region of the right greater trochanter.

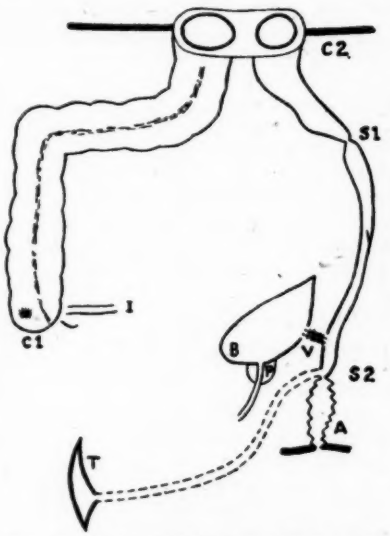

FIG. 1.—A, Scarred anus and anal canal. B, Bladder. C 1, Caecostomy. C 2, Transverse colostomy. I, Ileum. P, Prostate. S 1 and S 2, Strictures. T, Abscess over right greater trochanter. V, Obliterated vesico-colic fistula.

The right greater trochanteric region was slightly tender and swollen, but was not red or hot. After sigmoidoscopic examination of the distal loop of the colostomy, crepitus was easily elicited over this trochanter. The anus and the perianal tissues were scarred and tender (Fig. 1). Six centimetres from the anus the lumen was almost completely blocked by a stricture. Radiography of the hip showed an irregular erosion of the right greater trochanter.

Four months after this examination a purulent discharge appeared in the anus and was increased by pressure over the right greater trochanter. After another four months—that is, on December 13, 1949—the transverse colon to the left of the colostomy, the descending colon, most of the sigmoid colon, and their mesenteries were removed through a midline wound. The upper end of the remaining lower portion of the bowel was brought out above the pubis as with a first-stage Lahey resection of the rectum. Many adhesions were present in the pelvis at that time, and it was quite impossible to determine the extent of any intrapelvic infection. Normal haustrations were present in the right side of the colon. Convalescence after this operation was uneventful except for sloughing of a portion of the bowel in the suprapubic wound. He was discharged home on January 4, 1950, with the wound healed and with a small suprapubic sinus communicating with the rectum.

In the next 12 weeks his general condition improved, and on March 28 a perineal excision of the rectum and the lower end of the sigmoid colon was performed. At this operation considerable scarring and fibrosis of the ischio-rectal fossae and the perirectal tissues were encountered. The fistulous track leading into the right ischio-rectal fossa was followed backwards into the space between the sacro-spinous and sacro-tuberous ligaments. From there it appeared to take the path shown in Fig. 2. The vesico-colic fistula appeared to be healed although the rectum was firmly adherent to the bladder. Two weeks after operation he was discharged home with the suprapubic fistula healed and with the perineal wound healed except for the anterior half-inch (1.3 cm.). The latter discharged slightly and did not close for another four months. Since then there has been no further discharge from the perineum.

Within a few weeks of this operation the swelling, tenderness, and crepitus over the right greater trochanter gradually decreased. On only one occasion since then, and that 18 months afterwards, has he complained of any discomfort in the right thigh; and this vanished after a few days and has not reappeared.

When he was last examined on February 19, 1953, his general condition was excellent. The colostomy was acting only a couple of times a day. However, the mucosa of the right colon was redder than when first examined nearly three years previously, and the vascular pattern was no longer visible. No ulceration of the mucosa or stenosis of the lumen of the bowel was present, and its lumen did not contain any blood, pus, or excess of mucus.

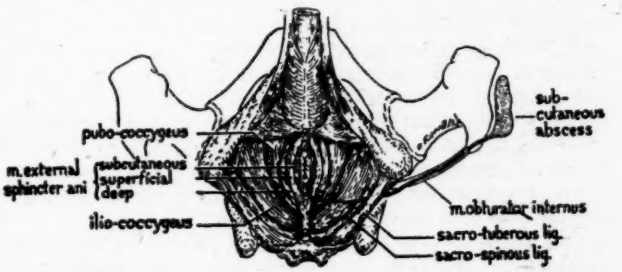

FIG. 2.—The abscess over the greater trochanter appeared to be subcutaneous, but this area was not explored, and it is more likely that it was situated beneath the deep fascia.

Discussion

Spread of an anal fistula beyond the perineal region is most uncommon unless it is complicated by or is due to a more serious lesion—for example, carcinoma of the rectum or chronic ulcerative colitis; and in this case the latter was the cause. Normally, the whole of the tracks of a fistula-in-ano should be laid open and the wound "de-roofed" and "saucerized." In this case such was not possible, but excision of the cause of the fistula, the infected bowel, together with the internal opening, would appear to have resulted in its cure. Drainage of the abscess in the thigh by a local incision was contraindicated prior to the resection of the rectum and anal canal, and since then it has no longer been troublesome.

When this patient first came under my care there was already a transverse colostomy, and the disease was apparently limited to the left side of the colon and rectum. It was accepted then that eventually he would probably need a total colectomy and an ileostomy. Yet, altogether, he has had nine years with the colostomy, and there is no evidence that his progress during that time would have been improved by an ileostomy. Until an ileostomy finally becomes necessary, as it probably will, he will have had many years of extra comfort.

The most important lesson to be learnt from this case is an old one—that is, the wisdom of avoiding minor rectal operations (haemorrhoidectomy, fistulectomy, etc.) in the presence of chronic ulcerative colitis.

Concluding a favourable review of the B.M.A.'s *Refresher Course for General Practitioners*, Dr. André Plichet, Editor of *La Presse Médicale*, writes in the February 28 issue: "The book is easy to read, because the authors have taken the trouble . . . to convert the outmoded English system of weights and measures into the metric equivalent." Copies of the book may be obtained from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, price 25s.

POLYPOSIS OF SMALL INTESTINE WITH PIGMENTATION OF ORAL MUCOSA

REPORT OF TWO CASES

BY

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The following cases are recorded as further examples of this condition. They both came to hospital with symptoms of intestinal obstruction due to intussusception, one having had two previous operations for a similar condition. The typical pigmentation in the oral region was present in each case.

Case 1

A housewife aged 26 attended hospital complaining of attacks of lower abdominal pain for the previous six months, increasing in frequency and severity. On two occasions she had vomited during an attack. She had no disturbance of bowel function and had noticed nothing abnormal in the stools. Micturition and menstruation were normal, she had not lost weight, and had had no previous gastro-intestinal trouble, nor had anyone else in her family.

She was a well-built woman, dark, with a rather sallow complexion. On the circumoral skin there was a well-marked irregular dark brown mottling which extended over the mucous membrane of the lips and the cheeks, where the patches were more numerous. This had been present as long as she could remember and had not changed in any way during the time. No similar pigmentation was found elsewhere on the skin or the vaginal and rectal mucosa. The only other abnormality found was an elongated tumour in the left iliac fossa which was not tender and which varied in size and position during the course of the examination. A provisional diagnosis of recurrent intussusception was made, and she was admitted to hospital 48 hours later.

There was then a smaller and rounder mass in the right iliac fossa which was very mobile and disappeared completely after palpation. The attacks of pain were now much more frequent.

Laparotomy was carried out through a lower right paramedian incision. There was no free fluid in the peritoneal cavity. In the upper third of the ileum an intussusception was found which reduced easily, and after reduction three polyps about 1 in. (2.5 cm.) in diameter could be felt in the lumen of the bowel, one having been at the apex of the intussusception. In the lower ileum there was a Meckel's diverticulum 2 in. (5 cm.) in length and, just distal to it, a second intussusception with a further polyp rather larger than the others. The rest of the small intestine and the colon appeared normal and no other tumours were palpable. About 7 in. (18 cm.) of ileum, including the diverticulum and the polyp, was resected and a lateral anastomosis made. A similar length, including the tumours in the upper ileum, was removed, and an end-to-end anastomosis made. Her convalescence was uneventful, and she has so far had no further symptoms.

The four polyps removed showed no evidence of malignancy on histological examination.

Case 2

A housewife aged 35 was admitted to hospital complaining of intermittent abdominal pain and the passage of dark tarry stools for the past six days. In 1939 she had been admitted to this hospital with an intussusception, and 20 in. (50 cm.) of small intestine containing five polyps had been resected. In 1943, at another hospital, a second resection for an irreducible ileo-ileal intussusception had been done but no polyps were found at this operation. Apart from these two incidents her health had been normal.

She had a much lighter complexion than the first case, but the pigmentation was of similar distribution over the inner surfaces of the cheeks and lips, although less marked on the circumoral skin. She was sure the condition had been present since childhood and had never noticed any change in it. There was no other pigmentation of the skin or of the rectal or vaginal mucosa. Apart from the two operation scars nothing abnormal was found on examination. A barium meal and follow-through *x*-ray examination showed dilatation of some loops of jejunum, suggestive of a subacute obstruction.

Laparotomy was carried out on the following day through a right paramedian incision. No free fluid was found. There was slight distension of the upper jejunum, and about 12 polyps could be felt along the course of the small intestine, one, larger than the rest, causing an intussusception in the upper ileum which was easily reduced. This polyp was excised with a small wedge of intestinal wall. In the lower part of the jejunum a 15-in. (38-cm.) length containing four polyps close together was resected with end-to-end anastomosis. No tumours were felt in the colon, but there was a complete intussusception of the appendix, which was reduced and the appendix removed. It contained three polyps. Histological examination showed no evidence of malignancy in any of the tumours.

She had an uninterrupted convalescence, and has so far remained free from further symptoms.

Comment

Although living in the same district, these two patients are not related. There is no evidence of pigmentation or polyposis in the family of Case 1. The second patient came to this country from Central Europe before the war, and further investigation is not possible, but she knows of no one else being affected in her family.

Four of the 27 cases so far recorded have been in this country—a father and daughter (Foster, 1944), a girl of 16 (Tanner, 1951), and a man of 50, originally operated on for intussusception in 1922 (Wolff, 1952).

Jeghers *et al.* (1949) have described the condition very fully, recording 10 cases of their own, and have shown the familial incidence in several of them and in the original cases of Peutz, in which three generations were involved. The presumptive evidence of polyposis is very strong in a number of cases with the characteristic pigmentation, including one of twins described by Jonathan Hutchinson (1896), Parkes Weber (1919), and two relations of Foster's cases. Wolff describes the typical pigmentation round the mouth and also on the hands in several relatives of his case, including one who died after an intussusception. Renyard (1951) also describes a case of gastro-intestinal polyposis with a number of small brown patches on the lower lip.

The pigmentation is either present at birth or appears in early childhood, and the intestinal symptoms usually appear by the third decade, as in the two cases described here. Polyposis without pigmentation is relatively common, but Jeghers *et al.* state that they have been able to find only one case of typical pigmentation with no evidence of polyposis, a woman of 57 years.

Intussusception of the appendix, as found in Case 2, was described nearly 100 years ago, but only about 90 cases have been recorded since, and Wakeley (1939) considers that the condition is probably much commoner than this would indicate. Various causative factors have been suggested, including foreign bodies, lack of meso-appendix, and enlarged lymphatic nodes, as in the ileo-caecal variety. I can find a record of only five cases due to polyps (McSwain, 1941), although polyposis of the appendix is not very infrequent.

I wish to thank Mr. V. Glendining, who operated on these cases, for his help and advice, and Dr. White Phillips for the *x*-ray report.

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Medical Memorandum

Recurrent Intussusception Due to Polyposis of the Gastro-intestinal Tract Associated with Pigmentation

The intussusception, gastro-intestinal polyposis, and pigmentation of skin and buccal mucosa sign-complex was first described by Jeghers (1944) and further elaborated by Jeghers *et al.* (1949). Tanner (1951) reviewed the literature and added a further case. Since then, so far as we have been able to ascertain, only two more cases have been reported (Schaffer and Sachs, 1952; Wolff, 1952), bringing the total number of recorded cases to 27. The following case, to the best of our knowledge, is the first to be reported from the Middle East.

The salient features of the syndrome, as borne out by all the reported cases, are: (1) The patients are usually of dark complexion. (2) Pigmented spots are present on the buccal mucosa, lips, and face, and sometimes on the digits. The spots vary in colour from "light brown on the face to dark blue-black on the mucosa" and have been shown to contain melanin. (3) The presence of gastro-intestinal polyposis, predominantly in the small intestine. The polyps are usually benign, but in one case malignant change has been reported. (4) The condition usually presents as recurrent intussusception in the second decade of life. (5) It is often familial, and is believed to be transmitted as a Mendelian dominant.

CASE REPORT

A boy aged 16, who was born in Turkey and had come to Israel in 1950, was admitted to the department of surgery on October 1, 1952, complaining of generalized abdominal pain associated with anorexia and vomiting, following the passage of a hard stool some four to five hours previously. The pain was colicky in nature, maximal in the epigastrium, and radiated to the left flank. Nausea was persistent and he had vomited several times after the onset of the pain. The vomitus contained undigested food. No blood was present in the stools and there was no history of recent diarrhoea. He had had an almost identical attack two weeks previously, when he was admitted to another hospital and discharged 48 hours later, his symptoms having subsided.

He had been well until 18 months earlier (March 8, 1951), when he was admitted to this hospital complaining of abdominal pain, constipation, vomiting, and the passage of red blood in his stools. On laparotomy an "ileo-ileal intussusception with a polyp about the size of an apricot" was found. The pathological report was that of a "benign polyp of the small gut." On discharge from hospital he continued to have attacks of abdominal pain with occasional bloody stools at approximately weekly intervals.

On August 9, 1952, he was readmitted with abdominal pain, constipation, vomiting, and blood in his stools. A laparotomy was again performed the day after admission, and "ileus due to adhesions related to the ileum and herniation of bowel through a deficiency in the omentum" was reported. After his discharge (nine days later) he was relatively well until the attack two weeks before his present admission to hospital. His mother, father, two brothers, and two sisters are all healthy and have no history of abdominal symptoms or operation.

Examination revealed a dark-complexioned youth, physically underdeveloped for his age—weight 73 lb. 11 oz. (33.4 kg.), height 4 ft. 10 in. (147 cm.). No pubic or axillary hair was present. The genitalia were small and undeveloped and the voice was high-pitched. Small pigmented spots about the size of a pinhead were present over the bridge of his nose and around his mouth. Larger bluish-black macular spots varying in size from 1/16 to 1/4 in. (1.6 to 6.4 mm.) in diameter were present on his lips and buccal mucosa, particularly the lower lip and the inside of the left cheek. No other pigmented spots or papillomata were found on the rest of the body surface. In the abdomen a sausage-shaped mass extending from the left flank to the left of the umbilicus was clearly palpable. Generalized abdominal tenderness was present, but no guarding or rigidity. No free fluid was detected, and the liver and spleen were not palpable. Rectal examination was negative.

A diagnosis of intussusception was made. At laparotomy a jejuno-jejunal triple intussusception was found involving about 1.5 m. of small bowel, with a large polyp (about ¾ in. (1.9 cm.) in diameter) at the tip of the intussusception. Resection of 10 cm. of bowel, including the polyp, was performed and the specimen sent for section. The pathological report was of a "benign adenomatous papilloma."

The patient made an uneventful recovery. A barium meal and follow-through, and a barium enema at a later date, showed no radiological evidence of further polyposis. On rectoscopy, however, a cluster of four sessile polypi, each about ¼ in. (6 mm.) in diameter, was seen on the left lateral rectal wall 9 cm. from the anal verge.

A subsequent examination of the patient's parents and siblings revealed no pigmentation of the buccal mucosa or skin in any of them, nor signs of polyposis of the bowel.

We wish to express our thanks to Dr. N. Rabinowitz, of the department of surgery, Hadassah University Hospital, for permission to report this case, and to Dr. Charlotte Kaplan for drawing our attention to this interesting but rare syndrome.

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Since its inception in 1947 the National Corporation for the Care of Old People has devoted its resources principally to assisting voluntary organizations by means of grants-in-aid to provide homes, clubs, and welfare centres. Its annual report for 1951–2 records that £116,515 was allocated in this way during the year, making a total of £790,000 during the last five years. The Corporation opened a rest home at Stanmore to admit patients discharged from the geriatric unit of West Middlesex Hospital and from Edgware General Hospital. Another home was opened at Greenisland, near Belfast, and a third is planned for Oxford. An experiment in Bristol was the provision in 1951 of a laundry service for old people. The Corporation, which has power to accept trusteeship of charitable bequests made to benefit old people, pleads that they "should not be regarded as a class apart, as objects either of pity or charity, but as people who with help can retain their independence and make their own contribution to the general welfare." The welfare of old people is also the concern of a special committee of the National Council of Social Service, whose annual report for 1951–2 records its activities. It makes available to Government departments, voluntary societies, students, and others up-to-date information and experience affecting the welfare of old people. At its national conference at Scarborough in 1952, 400 delegates heard Sir Walter Monckton outline the steps taken by the Government to ensure a new and sympathetic approach to the employment of the elderly on the part of employers, trade unions, and the public.

Reviews

CLINICAL NEUROLOGY

Clinical Neurology. By Frank A. Elliott, M.B., Ch.B., F.R.C.P., Professor Brodie Hughes, Ch.M.(Birm.), F.R.C.S., and J. W. Aldren Turner, M.A., D.M.(Oxon.), F.R.C.P. Edited by Frank A. Elliott. (Pp. 751. £2 2s.) London: Cassell and Co. 1952.

This book is "intended for those who are undergoing post-graduate training in medicine rather than for the junior student or the professed neurologist," and to this end it attempts "to present the common problems of neurology within a reasonable compass and to avoid the rare, the recondite, and the contentious."

In general, it follows orthodox lines. The first section is devoted to the principles of neurological diagnosis and includes essential anatomy and physiology, the mechanism of certain major symptoms, and methods of examination, including special diagnostic techniques, to which Dr. A. E. Ritchie contributes a useful section on the electrodiagnosis of neuromuscular disorders. The second section is on individual diseases. The text is throughout clear, concise, and unambiguous and the information sound and up to date. To each major section is appended a brief list of original papers which the reader might consult with profit. Nearly all of these are in English, but a few classical papers in French and German are included.

The growing contribution of neurosurgery is recognized by the admission of a surgeon to full partnership in the trinity of authorship. Professor Brodie Hughes is solely responsible for the sections on abscesses, aneurysms, vascular malformations, and tumours of the brain and cord and their adnexa, and shares responsibility for those on the examination of the patient and injuries to the head and spinal cord. All these are first rate. Other chapters which deserve special notice in an admirably balanced text are those on disorders of speech and language, mental disorders in organic disease, and infections of the central nervous system (though no treatment is given for Weil's disease). To 700 pages of text there are fifty of a most detailed and helpful index.

Useful additions to a future edition would be a section on occupational cramps (writer's cramp is mentioned only incidentally as a symptom of paralysis agitans), and references to the neurological manifestations of systemic lupus erythematosus, posterior interosseous neuritis (another "tunnel" syndrome), and the otolith syndrome, which are certainly not less common in Britain than cerebral schistosomiasis.

There is a notable absence of major typographical errors, but some of the minor defects and inconsistencies of multiple authorship are evident. On p. 186 tower skull is is called turricephaly; on p. 227 it becomes oxycephaly. Snippets of history are dispensed in some instances—for example, with tabes and G.P.I. (p. 357) but not with disseminated sclerosis or Parkinsonism. Sometimes capitals are used for all words in the nomenclature of disease—for example, Chronic Progressive Chorea (p. 252) and Parkinson's Disease (p. 525); in others this is modified—for example, Neuritic muscular atrophy (p. 247) and von Economo's disease (p. 323). Sometimes (Syn.: . . .), at others (Syn. . . .), and yet at others brackets only are used for synonyms; and, for example, in neurofibromatosis (p. 257), rabies (p. 337), and congenital spastic diplegia (p. 221) yet another form is seen. Moreover, "etc." should not occur among the synonyms (for example, p. 412).

The editor's claim that "eponymous terms have been avoided wherever possible" is hardly justified by the retention, even as synonyms, of such names as Fothergill's disease for tic douloureux, Swift's disease for erythroedema, Albl's ring for the calcification seen radiologically in the wall of an aneurysm, and Chastek paralysis for the lesions which silver foxes develop when fed on a diet of raw fish (what price "the rare, the recondite" here?). On the other hand, though a description is given of "the adrenal type" of fulminating meningococcal septicaemia, the common eponym Friderichsen–Waterhouse syndrome is studiously avoided.

These criticisms might well appear niggardly and trifling, so it must be emphasized that such minor blemishes are commendably few and do not detract from the excellence of a work whose intrinsic merits and handsome production ensure its place in the treasury of neurological textbooks for which English medicine is so justly famed.

HENRY COHEN.

PANCREATIC NEOPLASMS

The Surgery of Pancreatic Neoplasms. By Rodney Smith, M.S., F.R.C.S. (Pp. 157; 111 figures. £1 15s.) Edinburgh and London: E. and S. Livingstone. 1953.

Mr. Rodney Smith won the Jacksonian Prize of the Royal College of Surgeons of England with the essay that forms the substance of this book. In it he has presented an admirable review of this important subject at a time when just such a balanced and impartial assessment is needed. The operation of pancreatico-duodenectomy has passed from a hazardous procedure, successful only in the hands of a few pioneers, to an operation safe enough to be given a recognized position in orthodox operative surgery. The time has come for reassessment. And reassessment has shown that the prospects of cure in cases of malignant growth are much less satisfactory than was hoped at first.

In defining the problem, Mr. Smith states that the distinction between the so-called ampullary carcinomas and carcinomas of the head of the pancreas is of little practical value, and he deals with them together. But later, when he discusses symptoms and indications for operation, he admits the practical value of such a distinction, one that the majority of surgeons consider important. An ampullary carcinoma, whether it arises in duodenal mucosa, the lining of the ampulla, or the terminal bile duct, is a carcinoma that obstructs early and ulcerates early and is therefore recognized early. Further, being on the surface, it tends to spread superficially rather than deeply, to give radiological changes that are recognizable at an early stage, and to bleed early, sometimes so profusely as to call attention to its presence by profound anaemia.

The author presents the figures of Cattell, who has a greater experience of pancreatectomy than any other surgeon, and points out that in ampullary carcinoma the operative mortality is one-third that in carcinoma of the head, and the cure rate is 10 times as high. This is the experience of most surgeons, and, as Mr. Smith points out, the position to-day is that pancreatectomy for cancer of the head is attempted only when a careful preliminary mobilization fails to reveal any evidence of local or distant extension. Chapter XI, on the choice of operation, is admirable. Not everyone will agree with the statement that a one-stage resection is essential. Certainly any attempt at dissection, or any preliminary short-circuits, render the subsequent pancreatectomy almost impossible, but preliminary cholecystostomy, which does not interfere in any way with the operative field, has much to recommend it. A fortnight's drainage allows the liver to recover, and after resection the cholecystostomy removes the risk of leakage at the choledochojejunal anastomosis.

One reason why the surgical results in cancer of the pancreas are so bad is because the growth is clinically silent in its early stages, and radiological and biochemical investigations give little help. The author quotes two London radiologists as stating that they have obtained positive evidence by a barium meal in over 50% of cases examined; contact with two such optimists must have been a delightful relief from the hard work of preparing this book. The final sentence in Chapter VIII—"It is bad treat-

ment to allow an operation to be unduly delayed in order to carry out a number of tests"—brings back a cool blast of common sense. In Chapter XVII the author brings out well the sharp distinction betwen cancer of the body of the pancreas and that of the head—in symptoms, in the technical problems associated with the removal, and in prognosis. The leading symptoms are constant and unremitting severe pain referred to the back and loss of weight.

The book is admirably produced and embellished by well-chosen illustrations, many of them in colour. About the only criticism that can be offered is that Figures 4 to 9 illustrating variations in the blood vessels of the pancreas should be further explained; as they stand they are confusing rather than helpful. But this is a small defect in a book which will be of the greatest help to surgeons and essential to every library.

HENEAGE OGILVIE.

RELIEF OF PAIN IN LABOUR

The Practical Management of Pain in Labour. W. D. Wylie, M.B., M.R.C.P., D.A. (Pp. 148; 42 figures. 18s. 6d.) London: Lloyd-Luke (Medical Books) Ltd. 1953.

Dr. Wylie shows an understanding of the practical problems of pain relief in labour that is somewhat unusual in the specialist anaesthetist, who rarely has the time to acquire much practical knowledge of the subject. Now that an increasing amount of midwifery is being done in hospitals this state of affairs is tending to change, and books such as this will undoubtedly be of the greatest value.

Dr. Wylie discusses pain in normal labour from the usual anatomical and pharmacological aspects and gives accounts of all the available methods now in use for mitigating it. In addition he considers in great detail the problems of pain relief during abnormal labour. The influence of an anaesthetist's general experience on problems peculiar to labour is seen when Dr. Wylie properly deprecates the use of thiopentone as an anaesthetic in these circumstances, and also in the prominence he gives to the danger, ever present in obstetric anaesthesia, of vomiting and its sequelae. The illustrations, though not numerous, are adequate, and in the main are reproductions of commercially supplied pictures and diagrams of apparatus. They are mostly gathered together in one group of pages in the centre of the book, an arrangement not always convenient for the reader. Altogether, this is a well-written, helpful, practical account of pain relief in labour as practised in Britain.

W. W. MUSHIN.

THE THYROID GLAND

Joll's Diseases of the Thyroid Gland. By Francis F. Rundle, M.D., F.R.C.S. Second edition. (Pp. 520; 165 figures. £4 4s.) London: William Heinemann Medical Books. 1951.

The Thyroid. By Professor T. H. McGavack, M.D., F.A.C.P. With a section on Surgery by Professor J. M. Winfield, M.D., F.A.C.S., and W. L. Mersheimer, M.D., F.A.C.S., and a section on History by Dorothy B. Spear, Ph.B., and T. H. McGavack. (Pp. 646; illustrated. £4 15s.) London: Henry Kimpton. 1951.

These two excellent books are almost exactly the same size in area and thickness, but they will appeal to different classes of reader. Traditional scholarship is well served by the new edition of "Joll," and, if little of the book was written by its original author, the complaints will be few. It is pleasing that Rundle, who could have written an excellent textbook under his own name, should have preferred to commemorate his old master at the New End Thyroid Clinic, for Joll was greater than the work he left behind him and deserves a memorial. Considering that the preface is dated November, 1950, the book is remarkably up to date. A lot of I^{131} has passed through the Geiger–Müller counters since then, but the references to radioactive iodine in diagnosis and treatment are full enough for the general reader. Neither this nor any other scientific consideration is allowed to alter the balance of an essentially clinical book, which gives an excellent impression of knowledge tested and illumined by the practical experience of its authors.

One can read Rundle for pleasure as well as profit. No one could *read* McGavack; the facts are too closely packed, the references too detailed and too numerous. It is astonishing how much information is given in so small a space, but because of this McGavack (though it is in fact a few ounces lighter) is heavier going for the reader than Joll. This is a book for the specialist, especially if he wants fundamental physiology, laboratory techniques, and the latest information (which cannot, in a book, be very recent) about radioactive iodine.

I think I would advise buying both books.

RAYMOND GREENE.

OBSTETRICS AND GYNAECOLOGY

Recent Advances in Obstetrics and Gynaecology. By Aleck W. Bourne, M.B., B.Ch.(Camb.), F.R.C.S., F.R.C.O.G., and Leslie H. Williams, M.D., M.S.(Lond.), F.R.C.S., F.R.C.O.G. Eighth edition. (Pp. 339; 92 figures. £1 7s. 6d.) London: J. and A. Churchill. 1953.

This justifiably popular book has reached its eighth edition in twenty-seven years, and the authors' zest and power to sift the wheat from the chaff remain as remarkable as in their first edition. In order to keep the total work the same size and yet to cover individual subjects adequately, the number of chapters is now reduced to eleven. Three of these are on new topics—hypertension and pregnancy, functional uterine haemorrhage, and intravascular thrombosis and embolism. The remaining chapters have been revised and brought up to date, and some of the revision is very extensive. Obstetric radiology is covered by Dr. E. Rohan Williams, and radiotherapy in gynaecology by Dr. W. M. Levitt.

All those specializing, or hoping to specialize, in obstetrics and gynaecology will welcome this book, although views on which chapters are most helpful and interesting will vary with the reader's taste. Some will give pride of place to the articles on lactation and on carcinoma of the cervix—both subjects on which ideas have changed and are changing rapidly. Others may prefer the accounts of weight change and water balance in pregnancy, or thrombosis and embolism. The concise review of the literature and the summing up to give some sort of practical guide are usually masterly, and carry that most important imprint, the authors' personality and experience. When space is limited, how difficult it must be to choose the subjects to be included in a work of this kind, to decide which advances are sufficiently consolidated to merit permanent recognition in this form, and which developments are so uncertain of future acceptance as to warrant discard. The choice made by Mr. Bourne and Mr. Williams will find favour in the eyes of large numbers of readers.

T. N. A. JEFFCOATE.

The well-known *Textbook of Medical Practice* edited by Dunlop, Davidson, and McNee has now reached its sixth edition (E. and S. Livingstone, Ltd., 50s.). All sections have been revised and many of them largely rewritten. New chapters have been included on chemotherapy, rehabilitation, the treatment of poisoning, and the chemotherapy of malignant disease. An unusual change is that the volume has been equipped with that essential feature a completely new index. Also appearing in its sixth edition is *Recent Advances in Pathology*, edited by Professor Geoffrey Hadfield (J. and A. Churchill, Ltd., 30s.). An attempt has been made to discuss in this edition disorders of function and their relation to general physiological principles. The section on endocrine organs has been completely rewritten, and the account of pulmonary diseases covers a wider field than in previous editions. *An Atlas of the Commoner Skin Diseases*, by Dr. C. G. Semon, has been revised for a fourth edition (Bristol: John Wright and Co., Ltd. London: Simpkin Marshall, Ltd. 75s.). All the 147 plates are in colour, and some new ones have been added.

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TUBERCULOSIS OF BOVINE ORIGIN

A difficulty with which anyone campaigning for safe milk in recent years has had to contend was the lack of modern information about the amount of tuberculosis attributable to infected milk. The well-known findings of Stanley Griffith are now 20 years old, and only a fresh survey could decide how far the position had changed since the early nineteen-thirties. Such a survey was undertaken by the Medical Research Council as part of an inquiry into the causes of an apparent increase in the death rate from tuberculosis in the early part of the war, and the whole of the findings in the three areas of Great Britain have now been published by the National Association for the Prevention of Tuberculosis.[1] The investigations covered the period 1943–5 in England and Wales, 1943–4 in Scotland, and 1945–50 in Northern Ireland, and consisted in typing tubercle bacilli from cases of non-pulmonary tuberculosis and pursuing detailed inquiries about the patients from whom they were derived. The number of strains examined was 994 in England, of which 261 (26.3%) proved to be bovine, 112 in Wales (19, or 17%, bovine), 1,051 in Scotland (228, or 21.7%, bovine) and 387 in Northern Ireland (16, or 4%, bovine). The fact that the Northern Ireland investigation was carried out later, and the inclusion in it of a very high proportion of cases of meningitis, render direct comparison with the other figures unjustifiable: it would nevertheless seem from these results that the prevalence of infection of bovine origin in Northern Ireland is much lower than elsewhere.

The main result of this survey is to show that tuberculosis of bovine origin has remained a serious problem. It can be calculated from the findings that in 1944 550 deaths in Great Britain from tuberculous meningitis and 1,050 from other varieties of non-pulmonary disease were due to bovine bacilli. This total of 1,600 annual deaths is not far short of the figure calculated from Griffith's results 20 years ago. To this, in any assessment of the effects of milk-borne infection, must be added the consequences of invalidity or disablement in many thousands of patients with non-fatal infections. Detailed study of the age and sex incidence, history of raw milk consumption, history of contact with another case, and geographical distribution brings out a number of interesting points. The most notable and significant change is in the age incidence. In Griffith's series the highest incidence of bovine infection in every part of the body separately considered was in the 0–4 age group. According to the recent findings the age during which non-pulmonary tuberculosis is most often due to bovine bacilli is now 5–9 years; indeed, there is a general shift towards a later age incidence, a substantial proportion of bovine infections being in patients of 15 and over. The percentages of bovine infection in cases of meningitis and surgical tuberculosis respectively were in England 28.6 and 50.5 at ages 0–4 and 35.4 and 53.7 at ages 5–9. In Scotland the corresponding figures were 17.9% and 51.3% at ages 0–4 and 10.2% and 70.8% at ages 5–9. Why meningitis in Scotland alone should retain the older age distribution is unexplained.

There are several other minor discrepancies or differences of this kind between the findings in the several reports. Changes in feeding habits seem to provide the correct explanation for the more frequent occurrence of bovine infections in older children in recent times. Whereas in earlier days infants were often fed on cow's milk of doubtful quality, the efforts of welfare clinics have led to the introduction of systems of infant feeding with dried or other safe forms of milk, and the risk at this age and for some time after it, when similar foods continue to be used, is thus much diminished. On the other hand, the milk-in-schools scheme has led to a greatly increased consumption of milk from the age of 5 onwards, and some of this is still neither tuberculin-tested nor pasteurized. That the risk is not confined to childhood is illustrated by the fact that 30% of bovine infections in the English series were in patients aged 15 and over. The report also emphasizes that prolonged and regular consumption of raw milk is not always necessary to produce overt infection: inquiries into milk-drinking histories sometimes showed that its consumption can only have been "slight or occasional." Perhaps this evidence should not be accepted too literally: those questioned had to think back for some years, and a surprising number of intelligent people do not know whether the supply to their homes is pasteurized even at the time when they are asked about it. This report nevertheless affords strong support to the case for the general pasteurization of milk from any but T.T. herds.

[1] Wilson, G. S., Blacklock, J. W. S., and Reilly, Lilian V., *Non-pulmonary Tuberculosis of Bovine Origin in Great Britain and Northern Ireland*, 1952, London.

DISTRIBUTION OF DOCTORS

The fourth report of the Medical Practices Committee, a summary of which is to be found in the *Supplement* of this issue, has just been received by executive councils of England and Wales. It covers a period of 18 months up to the end of 1952. This interesting document contains an analytical survey of the movement of general practitioners since July, 1948, and for the first time an attempt has been made to assess the effectiveness of "negative direction" upon the distribution of doctors. The committee admits that it is rather early for such an assessment. Some of the figures are for various reasons not wholly accurate, and four and a half years is hardly long enough for general practice to have shaken down in the Health Service environment: but the committee thinks that now is the time to look back before entering the new era of the Danckwerts award and the Working Party's scheme, which, in the words of the report, "are bound to have rapid effects on the distribution of medical manpower."

The figures given in the report illustrate clearly the relative changes in the distribution of doctors since 1948. The average size of list throughout the whole country was 2,461 in 1948 and 2,430 in 1952. This reduction is not big, but the wide discrepancies in the average size of list which were evident in different parts of the country have narrowed. In 1948, for instance, the average in Radnorshire was 1,120, while in parts of Glamorganshire it was over 8,000: in 1952 these figures had become 1,320 and 2,832 respectively. In 1948 there were 6,648 principals with average lists of 3,163 in areas where the average lists were high. By January, 1952, the picture had changed to 7,397 principals with average lists of 2,869: this represents an increase of 11% in the number of principals practising in these areas. Conversely, in areas where the average lists were low in 1948 there has been a 10% reduction in the number of principals and an increase in the average list from 1,648 to 2,010. This shift in distribution is clear evidence that the powers given to the Medical Practices Committee under the Act have been used effectively.

A reflection on the effect of the Danckwerts award and Working Party's scheme on partnerships is to be found in the report: "From the numbers of new partnerships of which we have been notified each week since July last we know that the process of assimilating doctors into general practice in this manner (partnership) has again been restored to a satisfactory level. During the next few months the number is likely to exceed those hitherto admitted during any similar period." Again: "As a result of the Working Party's report, an increasing tendency for assistants in the larger practices to be taken into partnership has been noticed." The number of full-time assistants, other than trainees, dropped from 1,724 in 1951 to 1,566 in 1952. This is encouraging news to all who think that the best way of entry into general practice is by way of assistantship to partnership.

The task of the Medical Practices Committee is not easy. Its decisions must at times be unpopular and open to the criticism that a central body cannot be entirely conversant with local needs. In particular the task of reclassifying areas undertaken by the committee last year might well have led to disagreement with local executive councils and local medical committees. The fact that views were reconciled more easily than expected is a tribute which the central committee gladly pays to the local bodies. All this emphasizes the tact and understanding with which the Medical Practices Committee and its officials did their job.

THROMBOCYTOPENIC PURPURA

A useful introduction to the study of this disease is given in a review of eighty-nine cases by Hirsch and Dameshek,[1] since it provides what is so often lacking in otherwise comprehensive clinical accounts—a clear picture of the natural history of the disease. They define as "idiopathic" those cases of thrombocytopenia in which there is a normal or increased number of megakaryocytes in the bone marrow, and an absence of splenic disease and of conditions affecting the red- or white-cell precursors. Among the cases satisfying these conditions, two sharply differentiated groups were apparent.

The first group, consisting of 18 patients, was characterized by an acute onset of purpura haemorrhagica which subsided spontaneously in a few weeks or months. In 11 of these patients there was a probable aetiological factor such as a virus infection or the taking of a toxic drug before the onset of purpura. The second group consisted of 52 cases of chronic thrombocytopenic purpura in which haemorrhagic symptoms had persisted with fluctuating severity for many months or years, with no complete remission. Aetiological factors were not apparent in the majority of these patients, though in some cases chronic drug intoxication was possible.

It is clear that the recognition of these two varieties of thrombocytopenic purpura is important. In the first (acute) group splenectomy is probably contraindicated, since the condition is self-limiting. Transfusions of fresh blood, preferably taken by means of silicone-coated apparatus, have been found beneficial in tiding

the patient over the worst episodes. It is pointed out that reports of supposedly favourable responses to A.C.T.H. or cortisone may refer to its use in this type of naturally remitting thrombocytopenia.

In the chronic form of the condition only splenectomy seems to be of any real benefit, and the patient is likely to suffer from more or less severe haemorrhagic episodes until it is performed. Of 45 patients whose spleens were removed, 20 were cured, 10 received no benefit, and 3 died, while the remaining 12 survived the operation but were not followed up for a sufficient time to determine its effect.

Much remains to be learned about the aetiology of thrombocytopenic purpura. It is probable that in 11 of the 18 cases of the acute disease reported by Hirsch and Dameshek some toxic or infective process caused the thrombocytopenia, which was relieved when the toxic drug was withheld, or when the infection subsided. It is likely that in the remaining seven patients a similar but unidentified mechanism was operating, particularly as a blood eosinophilia or lymphocytosis was a feature of these acute cases.

Drugs had also been taken by a number of the patients suffering from chronic thrombocytopenia, and one patient was a habitual consumer of "sedormid." Some cases, at least, of chronic thrombocytopenia may be due therefore to chronic exposure to some toxic process. In this connexion the work of Ackroyd[2] is of the greatest significance. He has shown in thrombocytopenia due to sedormid that there is a factor in the patient's plasma which is capable *in vitro* of destroying platelets, provided that sedormid and complement are both present. It is probable that sedormid forms with the platelets an antigenic complex to which the sensitive patient produces an antibody, and this complex is destroyed by the antibody in the presence of complement. A similarity to the mechanism of haemolysis in acquired haemolytic anaemia is at once apparent. This similarity is emphasized by the observation of Evans and Duane[3] that thrombocytopenia occurred in a number of patients suffering from haemolytic anaemia, and by that of Wright and colleagues[4] that in six cases of "essential" thrombocytopenia there was evidence of an antibody coating the red cells. Evans and his colleagues[5] have been able to demonstrate agglutination of platelets by the sera of some patients with "essential" thrombocytopenia purpura. The possibility that idiopathic thrombocytopenia is in many cases due to the presence of a lysin, damaging both platelets and megakaryocytes, and sometimes also the red cells, must be seriously considered. The finding by Harrington and co-workers[6] that thrombocytopenia and purpura occur in normal subjects receiving transfusions of blood from patients with idiopathic thrombocytopenia could be explained by the presence of such a lysin in the transfused blood. The effect of splenectomy might therefore be the same (though still unexplained) in both haemolytic anaemia and thrombocytopenic purpura.

Lastly, these observations give some information on the mechanism of the haemorrhagic state in the purpuras. Ackroyd's finding that the local application of sedormid to the skin of sensitive patients caused purpuric haemorrhage in the area of application proves that a local vascular lesion is produced by the toxic agent. Ackroyd suggests that sedormid may form a complex with the vascular endothelium, which is then susceptible to damage by the platelet lysin, and there is evidence that, antigenically, platelets and vascular endothelium are very similar. Any agent that damages platelets may therefore damage endothelium, and it is probable that the vascular damage, and not the thrombocytopenia, is the principal cause of the haemorrhage. The haemorrhagic manifestations of thrombocytopenic purpura may be temporarily alleviated by the transfusion of platelet-rich blood,[7] but the clinical improvement lasts up to 48 hours *after* the platelet count has relapsed to its original level. The platelets therefore exerted some indirect effect on the haemostatic mechanism in this experiment. Perhaps they absorbed from the circulation a lysin which impaired capillary function.

[1] *Arch. intern. Med.*, 1951, **88**, 701.
[2] *Clin. Sci.*, 1949, **8**, 235, 269; ibid., 1951, **10**, 185.
[3] *Blood*, 1949, **4**, 1196.
[4] *J. Lab. clin. Med.*, 1951, **37**, 165.
[5] *Arch. intern. Med.*, 1951, **87**, 48.
[6] *Proc. Amer. Soc. clin. Invest.*, 1951, April 30, p. 25.
[7] Stephanini, M., Chatterjea, J. B., Dameshek, W., Zannos, L., and Santiago, E. P., *Blood*, 1952, **7**, 53.

PLANT SEED HAEMAGGLUTININS

The existence of substances in the seeds of certain plants which agglutinate human and animal erythrocytes has been known for over 50 years, and in 1908 Landsteiner and Raubitschek[1] demonstrated that the extracts of seeds of some leguminous plants agglutinated the red cells of certain species of animals, whereas the red cells of other species remained unagglutinated. But not until 40 years later was it discovered that extracts of seeds could be used to distinguish the blood group characters of human erythrocytes.

Renkonen[2] studied 99 species of the family Leguminosae (pea family) and found that extracts of the seeds of 31 species had a non-specific agglutinating action against human red cells and that extracts of the seeds of six species had a specific action. Among the latter were extracts of *Vicia Cracca* (tufted vetch), which contained a powerful anti-A agglutinin, and extracts of *Lotus Tetragonolobus, Laburnum alpinum,* and *Cytisus sessilifolius* (broom) seeds which contained agglutinins reacting strongly with O and A_2 cells. An examination of the seeds of 262 varieties of plants belonging to 63 families by Boyd and Reguera[3] and of those of certain Egyptian plants by Boyd[4] revealed a number of other seed extracts which possessed a moderately specific agglutinating action. Several species of *Phaseolus* had a strong anti-A activity, and in particular *Phaseolus limensis* (Lima bean) var. *limenanus* was found to yield extracts which were completely, or almost completely, specific for erythrocytes of blood group A. No evidence

was obtained that any of the extracts acted specifically on the B, M, or N antigens or on those of the Rh system. Another source of specific and highly active anti-A agglutinins has been demonstrated by Bird,[5-8] who has examined the behaviour of extracts of seeds of *Dolichos biflorus*—Belgaum 1–1–8. The agglutinins from these seeds show a much greater affinity for A_1 and A_1B cells than for A_2 and A_2B cells, but Bird considers that the extract can be used as a substitute for human anti-A sera provided special care is taken and freshly prepared extracts are used. As a reagent for the differentiation of the subgroups of A the *Dolichos biflorus* extracts present advantages over absorbed human anti-A serum because of the large difference between the titres against A_1 and against A_2 cells; in tests on 200 Indian blood samples of groups A and AB complete correspondence was found between the results obtained with the seed extract and those obtained with human anti-A_1 serum. Extracts of *Vicia Cracca* seeds also react more strongly with A_1 than with A_2 cells, but this does not seem to be due to the presence of two antibodies, since absorption with A_2 cells was found to remove all antibodies against A_1 cells.[9]

The previous studies on plants of the family Leguminosae were repeated and extended by Cazal and Lalaurie[9] to cover 420 species. They found agglutinins reacting preferentially with O and A_2 cells in some species in the Genisteae and Loteae and agglutinins for A cells in some species in the Galegeae, Vicieae, and Phaseoleae, but they failed to find an extract which would react specifically with B cells. Agglutinins reactive to a fairly high titre with B cells have been reported, however, by Krüpe and Braun[10] to be present in extracts of seeds of *Sophora japonica*; the extracts also contain agglutinins reactive with A cells, but the authors have indicated that these can be removed by absorption.

Recently the specificity of certain of the plant seed haemagglutinins has been examined in terms of purified human blood group substances and simple sugars of known structure.[11] Aqueous extracts of the seeds of three species reactive with O cells were inhibited by H-substance and the agglutinins in one of these extracts, that of *Lotus Tetragonolobus*, were inhibited by α-methyl-L-fucopyranoside to a higher titre than by the H-substance and also, less strongly, by sugars possessing structures related to that of L-fucose. Human A-substance, and to a slight extent N-acetylchondrosamine, neutralized the anti-A agglutinins extracted from *Vicia Cracca* and Lima bean seeds. The agglutination of A or B cells by extracts of *Sophora japonica* seeds was found to be inhibited by either A or B substances and by N-acetylchondrosamine.

[1] *Zbl. Bakt., I. Abt. Orig.*, 1908, **45**, 660.
[2] *Ann. Med. exp. Biol. Fenn.*, 1948, **26**, 66.
[3] *J. Immunol.*, 1949, **62**, 333.
[4] Ibid., 1950, **65**, 281.
[5] *Curr. Sci.*, 1951, **20**, 298.
[6] *Ind. J. med. Res.*, 1952, **40**, 289.
[7] *J. Immunol.*, 1952, **69**, 319.
[8] *Nature, Lond.*, 1952, **170**, 674.
[9] Cazal, P., and Lalaurie, M., *Acta Haemat. (Basel)*, 1952, **8**, 73.
[10] *Naturwissenschaften*, 1952, **39**, 284.
[11] Morgan, W. T. J., and Watkins, W. M., *Brit. J. exp. Path.* 1953, **34**, 94.

The discovery of agglutinins in plant seeds which exhibit human blood group specificity has suggested the possibility of their future use as reagents for routine blood group determinations in place of human iso-agglutinating sera, but it is too early yet to assess whether this will be practicable or advantageous. The demonstration of these agglutinins in seeds has, however, given further evidence of the wide distribution in nature of materials related serologically to the antigens and antibodies classified within the human ABO system and has provided useful additional reagents for studies on blood group specificity.

ENDEMIC GOITRE

In recent years the treatment of thyrotoxicosis by thiouracil and radioactive iodine has rather stolen the limelight from the immense problem of endemic goitre which has to be solved in countries scattered all over the world. In order to encourage Governments to investigate this common disorder and take steps to remedy it in their respective territories, the World Health Organization at the end of last year brought together a study group at the National Institute for Medical Research, Mill Hill. Fifteen representatives from Britain, Mexico, Australia, the United States, Yugoslavia, Switzerland, Holland, and India were welcomed by Sir Charles Harington, who has himself made such valuable contributions to the study of the thyroid gland. Sir Charles quoted these words from a memorandum[1] of the Goitre Subcommittee of the Medical Research Council:

> "The immediate cause of simple goitre is failure of the thyroid gland to obtain a supply of iodine sufficient to maintain its normal structure and function. This failure is usually brought about by an absolute environmental deficiency of iodine; it may also be caused by factors which interfere with the availability of dietary iodine or which impose an abnormal demand on the thyroid gland."

This simple exposition of the problem was reinforced by Dr. Kimball, who recounted his early experiences with the iodization of salt in Akron, Ohio, and later in the State of Michigan, where school surveys eventually showed the elimination of goitre.

The problem as it presented itself to some of the other members of the group was by no means so simple. In underdeveloped countries salt may be so crude or obtained directly by each individual that it is impossible to add iodide to it. Again, the salt may be so damp or stored in such hot and humid conditions that even when the iodide has been added it rapidly disappears. To add to the complications, some races may consume three times as much salt as others, or so it was claimed. The possibility of adding iodate instead of iodide to the salt was discussed. Iodate is much more stable, as Professor Murray's work showed, and is just as readily available to the thyroid, as Dr. Pochin neatly demonstrated by administering it in radioactive form

[1] *Lancet*, 1944, **1**, 107.
[2] Campbell, J. M. H., *J. Hyg.*, 1927, **26**, 1.
[3] *J. clin. Endocrinol.*, 1952, **12**, 191.

and then recording its collection by the thyroid gland. There have been few field trials with it, although at present it is being used in Guatemala. The study group inspected a simple plant designed for adding iodine to salt of any degree of coarseness. It would appear that the cost of such installations would be trivial compared to the saving made by eliminating so much ill-health of one kind or another.

Definite evidence was brought forward that endemic goitre was a cause of cretinism and that the incidence of deaf-mutism in affected regions was much increased. How far feeble-mindedness or retarded skeletal or sexual development could be attributed to endemic goitre was a subject tabled for further investigations. Undoubtedly the disease is responsible for much loss of productivity. In addition, many people have to be admitted to hospital for treatment, and in some countries there is a high incidence of hypoparathyroidism and laryngeal palsy after thyroidectomy. The only statistics available suggest that the death rate from hyperthyroidism is higher in areas of endemic goitre,[2] but the group came to no decision on whether thyroid cancer was commoner in goitrous communities. A plea was made that investigators should be sent from well-equipped laboratories to study individual patients in areas of endemic goitre. Modern methods, including radio-iodine, could be used with advantage, as Stanbury[3] recently reported after his visit to Mendoza, in Argentina. After seeing a series of autoradiograms, prepared by Selwyn Taylor, showing the evolution of nodular goitre, the group decided that this also would be a useful method of research in studying endemic goitre.

The World Health Organization has provided an excellent opportunity for the exchange of information and views on endemic goitre, which is obviously much more common than many people imagine. The study group's report should form a helpful guide to those countries which are faced with the task of eradicating this disorder.

RADIO-COBALT BEAM THERAPY

At a special meeting of the British Empire Cancer Campaign last week (see p. 669) the Duke of Gloucester announced that Britain is to receive from Canada, by the generosity of Mr. J. W. McConnell, of Montreal, a powerful cobalt-60 beam therapy unit of about 1,100 curie strength. The gift emphasizes the unity of purpose and co-operation in cancer research which exists throughout the Commonwealth. The apparatus will be primarily used for the treatment of deep-seated and inaccessible tumours—the group at present usually subjected to *x*-ray therapy.

Cobalt deposits occur naturally in the region around Ontario, and the radioactive isotope cobalt-60 results from the neutron bombardment of the natural element in an atomic pile. As the radio-cobalt (Co^{60}) decays to nickel (Ni^{60}) it emits gamma rays having energies of 1.17 and 1.33 MeV (million electron volts) and beta rays of energy 0.3 MeV. Thus a radio-cobalt source gives out penetrating rays which are almost monochromatic without filtration and of average energy just over a million volts, most of the beta rays being absorbed in the source. The half-life of Co^{60} is 5.3 years, so that in that time the source has decayed to half its original strength. Its physical properties are such that in many ways it is an attractive substitute for radium. Teletherapy units using radium ("radium bombs") have been restricted in strength not only by the cost of radium but also by bulk.

Units with radio-cobalt as the radiation source have been developed in Canada in recent years, and two units with over 1,000 curies of radio-cobalt have been in clinical use since 1951.[1,2,3] Johns,[1] who designed the 1,100-curie unit at the University of Saskatchewan, used as a source a radio-cobalt disk measuring 1 in. (2.5 cm.) in diameter and 0.5 in. thick; with a source-to-skin distance of 80 cm., this gives an output of 33 r per minute—which makes routine radiotherapy practicable. The cobalt decays at the rate of 1.1% per month, and treatment times are adjusted accordingly. Measurements of the dose of radiation at various depths[4,5] show that the distributions obtained with the cobalt-60 unit are similar to those with *x*-ray machines of 2–3 MeV maximum energy. A tumour situated 10 cm. below the surface receives between 50 and 60% of the surface dose, and, since the apparatus permits of multiple-field, beam-directed irradiation, very high "tumour doses" can be given. The advantages of the radio-cobalt unit compared with a 2-million-volt *x*-ray apparatus are, as Watson[2] points out, the low initial cost, low upkeep, the compactness and manœuvrability of the unit, constant output (subject to the constant decay), the homogeneous beam, and the higher depth dose. To set against these are the disadvantages of a lower output, and the fact that the cobalt, with a half-life of 5.3 years, will probably have to be replaced in about three years. The deep lesions suitable for this form of treatment would probably include carcinoma of the upper air passages, oesophagus, lung, female genital tract, and rectum.

Experience of supervoltage *x*-ray therapy in this country began in 1937 with the installation of the million-volt apparatus at St. Bartholomew's Hospital, and the advantages of increased depth dose, with diminished skin and constitutional reaction, are now well known. The radiotherapeutic problem of obtaining homogeneous ionization within the tumour-bearing volume, with sparing of normal tissues, is being pursued at a number of centres which are using higher and higher voltages. The energy range of 1–5 million volts still requires investigation by means of large-scale clinical trials, and the installation of this new unit at Mount Vernon Hospital, Northwood, under the auspices of the British Empire Cancer Campaign, will be an important event in clinical cancer research.

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[1] Johns, H. E., *J. Canad. Ass. Radiol.*, 1952, **3**, 2.
[2] Watson, T. A., ibid., 1952, **3**, 7.
[3] Smith, I. H., ibid., 1952, **3**, 16.
[4] Johns, H. E., Epp, E. R., Cormack, D. V., and Fedoruk, S. O., *Brit. J Radiol.*, 1952, **25**, 302.
[5] Dixon, W. R., Garrett, C., and Morrison, A., ibid., 1952, **25**, 314.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

CONVULSIONS IN CHILDHOOD

BY

BERNARD SCHLESINGER, M.A., M.D., F.R.C.P.

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In discussing fits in childhood the first point to make quite clear is that on many occasions they have not the same serious significance as in adults. The central nervous system of some infants and older children is more unstable than that of others, so that unusual brain stimuli easily evoke convulsions which under similar circumstances would never appear at a more mature stage.

Symptomatic Fits

One large group can be labelled "symptomatic." These cases should be recognized as early as possible so that a series of fearsome investigations and gloomy prognostications can be avoided. A history of some infection or febrile disturbance each time the convulsions arise is suggestive, and in doubtful cases help can be obtained from an electroencephalographic tracing. For a few days a sedative should be prescribed to cover any possible recurrence during the fever, and instructions given that the drug can be repeated as a prophylactic measure in the event of another acute infection. Symptomatic fits are particularly apt to occur in infancy, and again towards puberty.

Apart from this important group, which must always be excluded first, fits in children can be classified into the following aetiological categories: traumatic, metabolic, hypertensive and toxic encephalopathy, degenerative, cases due to infection of the central nervous system or to raised intracranial pressure, and epileptic.

Vascular Damage

Traumatic fits are mostly encountered in the neonatal period. They are associated with oedema of the brain or frank cerebral haemorrhage, due either to a stormy labour at full term or to the hazards of birth in a premature delivery. The clinical picture is characteristic: breathing is shallow or irregular; the baby is restless, "jumpy," or hypertonic; the fontanelle is tense; and the colour is poor or definitely cyanosed (asphyxia neonatorum). The main requirements are an atmosphere of 50% oxygen and sedation with chloral hydrate orally in ½-gr. (32-mg.) doses at four-hourly intervals, or with sodium phenobarbitone, ¼ gr. (8 mg.) eight-hourly intramuscularly. Lumbar puncture may reveal fresh or altered blood, but, since its discovery will hardly influence treatment at this stage, there is much to be said against carrying out this procedure. It is far wiser to disturb the infant as little as possible in the hope that any haemorrhage is slight and will cease spontaneously. A major tentorial tear will probably prove fatal whatever steps are taken.

Vascular accidents due to birth trauma sometimes have delayed symptoms. A *subdural haematoma*, for instance, may take some months to produce signs of a space-occupying lesion; it is discussed in fuller detail below.

Vascular occlusion, usually arterial, either by embolism or by thrombosis, may cause degeneration and atrophy of quite large areas of cerebral tissue, usually after an appreciable interval. As a result an apparently normal infant will suddenly develop a series of fits and serious mental deterioration at the age of 3 to 4 months, often associated with hemiparesis. Quite a number of these children survive and grow up with gross mental retardation. Some of them finally enter an institution, where years later necropsy may reveal a shrunken, "walnut" brain on one side. In some cases of infantile hemiplegia the intelligence is less impaired, but the fits increase in number and severity, and are not controlled by the usual sedatives. Recently hemispherectomy of the affected side of the brain has been attempted for this condition and successful results have been reported.

Sinus thrombosis is also best considered under this heading. It may be purely infective, as in the case of lateral sinus thrombosis, rare these days, associated with otitis media and mastoiditis. Ascending cortical thrombosis can arise from the same source, but it occurs more often in adults than in children. The sagittal sinus may also become thrombosed as a terminal event in a dehydrated marasmic infant who has suffered from a prolonged and intractable bout of diarrhoea. These vascular lesions can all lead to fits.

Metabolic Convulsions

Various metabolic disturbances can produce convulsions. A good example is *hypoglycaemia* in diabetes mellitus, when the amount of insulin is excessive or a child on an adequate maintenance dose refuses food during an acute illness. Protection can then be afforded with sweetened fruit drinks, which the child can usually be persuaded to take. *Hypocalcaemia* with tetany, laryngismus stridulus, and fits (spasmophilia) was a not uncommon complication of rickets in the past, but is hardly ever seen now, since the associated vitamin deficiency has practically disappeared in this country.

Very severe degrees of *alkalosis* can cause convulsions, but there are few clinical conditions which can lead to this, with the possible exception of prolonged vomiting or post-operative gastric drainage. If for any reason alkalis are also being given, particularly when there is dehydration and impaired renal function, the danger is greater.

Encephalopathies

Hypertensive encephalopathy is occasionally encountered in children, with fits as one of the main symptoms. It is one of the rare complications of acute nephritis (Type I); more often it is seen in the terminal stages of chronic nephritis or in congenital abnormalities of the kidney associated with renal rickets. When the condition is reversible, as in acute nephritis, every effort should be made to reduce the cerebral oedema. Magnesium sulphate, 1 to 3 oz. (30 to 90 ml.) of a 50% solution, can be given rectally, or, by intramuscular injection, 0.2 ml. of a 25% solution per kg. of body weight. Hypertonic solutions of glucose (50%) also help if given intravenously, 10 ml., repeated if necessary.

The only metallic poison likely to affect the brain in children is lead. There is usually a history of pica—a curious habit of eating dirt and other unusual substances. Plumbism can result from licking the paint off the side of cots or biting the heads off toy soldiers, as occurred in one of my cases. Eventually the child may go into a state of coma and die. Some recover but are left with fits and some impairment of their intelligence.

Degeneration

Apart from the vascular lesions already mentioned and the toxic effects just described, there are certain other degenerative conditions of the brain, such as amaurotic family idiocy and Schilder's disease, which may be associated with fits. Encephalopathy with resulting demyelination is also a recognized complication of vaccination and of several of the exanthemata.

Infection

Convulsions may also be due to infection of the brain or meninges. Virus encephalitis, encephalo-myelitis, bacterial meningitis, and, rarely, syphilitic pachymeningitis may begin in this way. Examination of the cerebrospinal fluid will assist the diagnosis and there may be other suggestive physical signs in the central nervous system. Lumbar puncture should not be lightly undertaken in the presence of papilloedema, for a brain tumour is then a possibility, with a pressure cone. Sudden release of cerebrospinal fluid may then prove fatal. If, therefore, in doubtful cases this investigation has to be undertaken, very little fluid should be removed and the operator should be prepared to inject sterile normal saline into the thecal canal immediately any alarming effects are noticed.

Localized Intracranial Lesions

Tumours of the brain situated supratentorially may give rise to convulsions as an early manifestation; in fact a Jacksonian epileptic attack may have some localizing value. Since, however, the cerebellum and pons are much more likely to become involved in children, fits are not often the presenting sign. The commonest site for *abscesses* is either the cerebellum or the temporal lobe, by direct extension from an infected ear or mastoid. Fits are therefore not a common feature, but they may result from pyaemic abscesses, which can develop anywhere in the brain. A more likely cause of fits from a localized lesion is a *subdural haematoma*. Its development from birth trauma has already been mentioned and also the delay before its presence is suspected. This is because it takes time for the haemorrhage to become fibrinized into a cystic tumour which absorbs fluid, gradually increases in size, and encroaches on neighbouring structures. The clinical picture then is that of progressive hydrocephalus with separation of the sutures and, in all probability, fits. Surgical removal of the cyst is followed by complete recovery. A blow on the head, seemingly insignificant at the time, may bring about the same sequence of events. Gross hydrocephalus from other causes may also produce convulsions, and for this reason fits usually occur in a rare protozoal infection—toxoplasmosis.

Epilepsy

This forms the largest group in any paediatric practice, and, although much can be done to control such fits, these cases are always likely to recur. Heredity plays a considerable part, but it is also possible for fits in one generation to be followed by migraine in the next and vice versa. Some indication of the outlook in epilepsy may be gathered from what occurred in a parent or elder brother or sister who suffered from similar trouble in childhood. If the disorder disappeared as they grew older, there is a reasonable prospect of the same happening in the child now brought for advice. Adie singled out a group of patients who suffered from innumerable attacks which were uninfluenced by any form of treatment. They appeared to be familial and tended to clear up at puberty (pyknolepsy).

Petit Mal.—This type of epilepsy is too well known to need detailed description. Difficulty in diagnosis may arise at first, since the lapse of consciousness may be so very brief as to pass unrecognized. The child may merely change colour momentarily or cease what he is doing and not resume where he left off. Two of my patients are particularly good examples of this. One boy was undressing to retire for the night, when he suddenly stopped and proceeded to re-dress himself and walk downstairs, thinking it was time to get up. The other, a young girl, set forth to fetch some milk from the local dairy. On her way she had her first "turn," with a brief gap in her train of thought. She never completed her errand and came home with an empty can. Parents sometimes bring their child because of "day-dreaming," which takes the form of a vacant stare into the distance for a few moments. Occasionally other epileptic equivalents are seen which make children behave in an odd way. The lapse of consciousness may be just long enough for a child with petit mal to lose his balance and drop forward from a sitting posture. Recovery is almost instantaneous, and when the fits are often repeated they resemble the obeisances of an old Indian servant, and hence have been called "salaam convulsions." For the most part, however, petit mal is easy to recognize, the short seizures becoming more and more frequent until a bad case may develop as many as 50 a day. The differential diagnosis is not difficult. At times asphyxial attacks as a result of breath-holding have been mistaken for minor epilepsy, but the fact that they occur only when the child is thwarted and in a temper tantrum is enough to give the case away. The remedy, a douche of cold water, is both simple and effective. A Stokes–Adams syndrome is exceptional in childhood, although rare examples have appeared in congenital heart-block. Sudden cerebral anaemia is more likely to occur in the severest forms of Fallot's tetralogy, with an asphyxial "black-out" on the slightest exertion.

Grand Mal.—Petit mal can continue for some years, but after a time it generally becomes interspersed by major attacks. The reverse is not seen; if children begin with major epilepsy, this is the type of fit which will be repeated. It has the same characteristics as in adults, sometimes with incontinence of urine at the time, and often with vomiting, headache, and drowsiness afterwards. Auras are not likely to occur or are not recognized as such. Temporary paralysis of a limb, or a unilateral extensor plantar response, persisting for some days after a severe and prolonged fit, is not uncommon (Todd's paralysis). Outside influences, such as an accidental knock or a fever, can also sometimes precipitate an attack. There may then be difficulty in distinguishing true epilepsy from a symptomatic fit, and the diagnosis will depend on whether other attacks have occurred spontaneously. Help will also be gained from an electroencephalogram, which in idiopathic epilepsy will show characteristic waves. Occasionally, epilepsy will begin in a Jacksonian manner, although later it will take on the more usual form.

Status epilepticus, in which one fit succeeds another for one or two days on end, is a most dangerous condition. Every step should be taken to terminate it, otherwise the child may succumb through sheer exhaustion and with a high temperature. In some cases there is irretrievable damage to the brain.

Treatment of Epilepsy

Many drugs have been tried in idiopathic epilepsy. Bromides have largely passed into disuse and their place has been taken by phenobarbitone, which is particularly useful in grand mal, but less effective in petit mal. For infants ¼ to ½ gr. (8 to 16 mg.) can be given twice a day as a maintenance dose; older children can take up to 1 to 3 gr. (65 to 200 mg.) a day according to age. Toxic signs will appear as ataxia, a rash, depression, and, occasionally, such excitability that the child will become difficult to control. Methylphenobarbitone has been claimed to be less toxic and so can be given in a dosage which is 50% to 100% greater. Phenobarbitone often fails in petit mal and then it is worth changing to phenytoin, ½ to 3 gr. (50 to 200 mg.) daily up to 6 years of age; 3 to 4½ gr. (200 to 300 mg.) over 6 years.

Troxidone and "paradione," a less toxic compound, have been recommended as specially useful in petit mal, but they can have alarming side-effects, and patients on these drugs should remain under careful medical supervision and have blood counts carried out fortnightly at first, and then at monthly intervals. Leucopenia with agranulocytosis, albuminuria leading occasionally to Type II nephritis, rashes, and digestive upsets are the chief complications. It is advisable to combine troxidone with phenytoin, as otherwise there is danger of the treatment provoking an attack of grand mal. The dose of troxidone is 0.3 g. daily in three divided doses up to 2 years of age; 0.6 g. daily from 2 to 6 years; and 0.9 g. over 6 years. My experience with this drug has not

been very encouraging. "Mysoline" has undergone quite recent trials with reported good results in major epilepsy. A suitable dose would range between 0.25 and 0.75 g. daily, but the treatment is still in the experimental stage, and the optimum dose for children has not yet been established.

It is obvious from this account that of the two types of epilepsy petit mal is the most difficult to control, and sometimes the older forms of treatment are still found to be effective. Tincture of belladonna, 10 minims (0.6 ml.), combined with sodium borate, 6 gr. (400 mg.), three times a day for a child of about 6 years, is worth trying, and when everything else fails a ketogenic diet may save the situation. This is made up with an adequate amount of protein and with the proportion of fat to carbohydrate and protein in the ratio of 3 to 1, the total calorie value being 50 to 60 per kg. per day, depending on whether the child is under or over 5 years of age. Obviously with the present rationing in this country it is not easy to maintain this diet out of hospital, but special permits can be obtained at the local food office.

The urgency of treating status epilepticus energetically should again be emphasized. Chloroform and rectal thiopentone (1 g. per 25 kg. of body weight, diluted to a 2½% solution with water) are only temporary measures. Intramuscular injections of paraldehyde, ½ to 6 ml., according to age, is certainly the most effective and may have to be repeated if the fits recur.

Vasovagal Attacks and the Periodic Syndrome

There remain two other disorders which have not so far been considered. Girls, particularly when they are approaching puberty, are sometimes brought to the doctor with a history of fainting. Some strain such as early morning devotions on an empty stomach may be found responsible, and in others it is an inadequately functioning vasomotor system with sudden changes of position which is at fault. In any case the nature of the attacks, the colour of the patient, and the absence of any immediate sequelae are enough to differentiate them from true convulsions. Much more difficult to determine are the short lapses of consciousness which sometimes occur in migraine, cyclical vomiting, and the rest of that syndrome, but these blackouts cease as the child grows up and never develop into true epilepsy. They are nevertheless largely prevented by phenobarbitone.

In conclusion it can be said that fits in children are a common event and have a distinctly varied origin. Many of them are merely an expression of some temporary disorder; others are of a more serious and permanent nature. Among the latter, heredity plays an important part which is not unknown to the laity as well as to the medical profession:

> Year by year in pious patience
> Vengeful Mrs. Boffkin sits
> Waiting for the Sleary babies
> To develop Sleary's fits.
>
> —RUDYARD KIPLING.

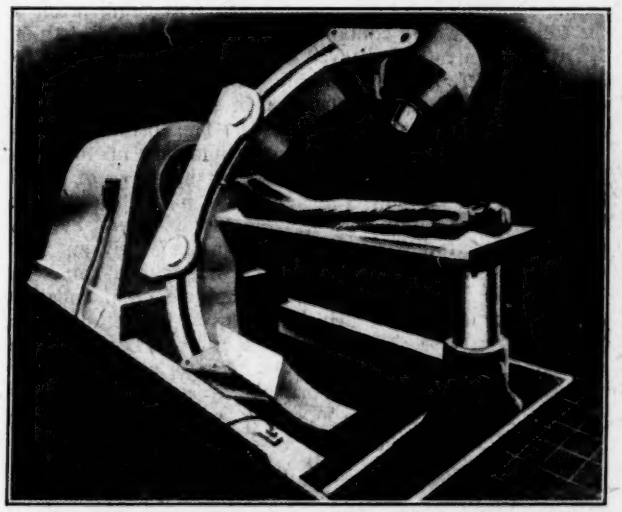
Next Refresher Course Article.—"Recurrent Boils," by Dr. S. T. Anning.

Some details of the scheme to establish medical hostels for industrial workers with rheumatism are given in the fifth annual report of the British Rheumatic Association. The first hostel was established last year at Northwood, in Middlesex, and when funds become available others are planned for Scotland, the industrial North, and the Midlands. Their object is to cut out long delays in waiting for hospital beds. Hostels will be sited near the rheumatic unit of a general hospital so that patients can start treatment at once. The hostels will be managed by the newly formed B.R.A. Homes Ltd., a housing society with charitable status. It is estimated that among miners alone absenteeism caused by rheumatism costs the country £15m. a year.

BEAM THERAPY GIFT TO CANCER CAMPAIGN

Presiding at a special meeting of the British Empire Cancer Campaign at the House of Lords on March 10, H.R.H. the Duke of Gloucester announced a generous gift to the Campaign of a cobalt-60 beam therapy unit. He said that the presence of considerable deposits of cobalt in Canada had led to large-scale experiments there on artificial radioactivity, and a few cobalt units for research into the treatment of cancer had been constructed in the Dominion. A unit had now been built incorporating all the improvements found desirable from experience with the earlier models, and it was this unit which had been presented to the Campaign. Sir Stanford Cade and Professor B. W. Windeyer, who visited Canada recently, had discussed the matter with their Canadian colleagues, and the financial difficulty had been removed by the action of one of Canada's outstanding philanthropists, Mr. McConnell, of Montreal, who had offered to pay for the entire unit himself at a cost of over £25,000.

His Royal Highness added that the unit was due to arrive in this country in August and would be installed at Mount Vernon Hospital, Northwood, after being first exhibited at the seventh International Congress of Radiology at Copenhagen in July. The Campaign had arranged for a prominent physicist, who would be one of those working with the unit when it was installed, to go to Canada next month to gain first-hand knowledge of its operation.



A Canadian artist's impression of the cobalt rotational beam therapy unit. (By courtesy of the British Empire Cancer Campaign.)

Lord Horder, Chairman of the Campaign, in expressing appreciation of the gift, said that this new apparatus made him feel how far they had travelled in radiophysics in the last 25 years. It also brought home the complexity and difficulty of this subject, the enormously increased cost of the armamentarium, and the demand which its effective operation made upon highly trained personnel.

The Minister of Health, Mr. Iain Macleod, said that this was the most massive weapon ever made in this field. He expressed thanks to all concerned, in particular to Mr. McConnell for his magnificent financial contribution, to Mr. Paul Martin, Minister of National Health and Welfare in Canada, for his co-operation, and to the British Empire Cancer Campaign for undertaking the care and operation of this unit. It was altogether a fine chapter in voluntary effort.

Cobalt in Radiotherapy

Sir Stanford Cade and Professor Windeyer then gave a brief exposition of the place of cobalt in radiotherapy. Cobalt-60, a radioactive isotope, said Sir Stanford Cade, was at present the most suitable substitute for *x* rays and

radium, and in small quantities it had been used in this country as such. The cobalt unit would be both a tool for research and an instrument for treatment. It was nearly 200 times as powerful as the radium units in use at present. Its depth dose of radiation was about the same as that of 3,000,000 electron volts of *x* rays, but it was more stable, more reliable, and simpler to control than a supervoltage *x*-ray machine. The primary object in view was to treat inaccessible tumours which so far had proved beyond the effective range of existing radiotherapy apparatus. A further advantage was that a greater quantity of radiation could be delivered to the tumour with less damage to surrounding normal tissues and less general disturbance of the patient.

Professor Windeyer said that the most obvious way for cobalt-60 to be used was as a replacement for radium in some of the apparatus for telecurie therapy, the so-called radium bomb. Some 10-gramme radium units—the largest yet to be used in Britain—had been replaced by cobalt in amount up to a maximum of 50 curies.

The first massive telecobalt unit had been installed in the Victoria Hospital, London, Ontario, in November, 1951, and at about the same time a similar one, constructed by the staff of the University of Saskatchewan, was installed at Saskatoon. These units contained approximately 1,100 curies of cobalt-60, which was the equivalent of about 1,500 grammes of radium. The unit which was being given to the Campaign would contain the same amount of cobalt-60, but it was a greatly improved model. It could be used for rotational therapy, for example. On both technical and economic grounds the construction of a radium unit of such activity would be quite impracticable. The cost alone would be well over £1m. and the radium would take up too great a space. The cobalt-60 source was in the shape of a disk only 1 in. (2.5 cm.) in diameter and ¼ in. (1.3 cm.) thick. The beam of radiation coming from the unit could be compared in penetration power to that produced by an *x*-ray machine working at 3,000,000 volts, but with a somewhat lower output. It must be realized, however, that cobalt-60 deteriorated to half its original intensity in just over five years, and it was therefore necessary to arrange for reactivation of the source in a nuclear reactor at regular intervals. In addition to the original apparatus in London, Ontario, and in Saskatoon, there was one working in Vancouver, and arrangements were being made for units of this new model to be installed in Toronto, Montreal, and New York.

THE ELDERLY "CHRONIC"

Every student of geriatrics knows that the population of this country has more than doubled during the last 100 years, but that the number of persons of 65 and over has increased between four- and five-fold. Consequently there are continual complaints of the economic burden which the producing community has to carry owing to the rising proportion of ageing persons. There are, however, two qualifications which are often disregarded: one that the ratio of workers to non-workers is more favourable than it was 100 years ago because the child population has diminished to a greater extent than the aged population has increased; and the other that life has not only been prolonged but made more healthy and active, so that in many instances people remain producers to a more advanced age than formerly.

Neither of these considerations has been lost sight of in an admirable report on the treatment and care of the elderly chronic sick in Bristol which has been compiled by the Bristol Local Medical Committee.[1] In 1950 a subcommittee was appointed by the committee to investigate the treatment and care of such persons. It soon found that it had to widen its reference to include the "frail ambulant" (i.e., the aged infirm person), the acute aged sick, and the healthy old person whose principal need is to be properly housed. The number of people over 65 in Bristol is about 50,000, and reckoning, as is usual, that 3% require to be accommodated in institutions of one kind or another, 1,500 beds would be sufficient to cover the need. By 1975, however, if present trends continue, the number of beds may be 2,400. At present two hospitals with a total of 800 beds are allocated to the aged and chronic sick in Bristol, and there are one or two small institutions outside which accommodate some of Bristol's overflow.

The report states that the hospital-bed situation could be relieved by the provision of non-hospital facilities, mainly through social service agencies, for the elderly infirm as distinct from the chronic sick. The recommendations mention such needs as diversional occupational therapy, help for old people to maintain a healthy diet, an adequate chiropody service, and friendly assistance in various matters. The almoner is considered to be the most appropriate person to act as liaison officer between hospitals, general practitioners, and other authorities, although objection is sometimes raised to almoners undertaking work outside hospitals.

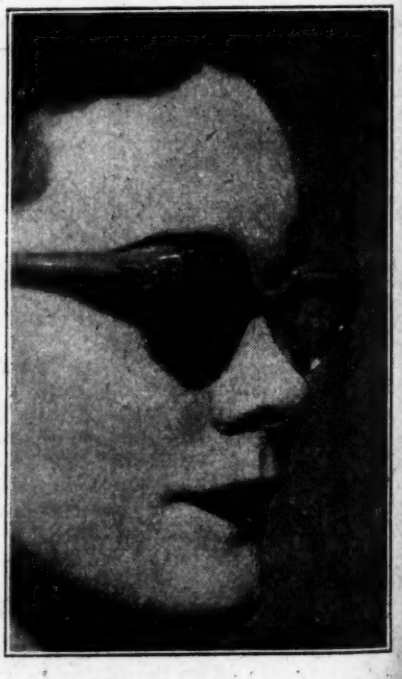
The division of responsibility between three sections of the National Health Service has complicated the problem. Hospitals are often unable to discharge patients because there is nowhere for them to go, and meanwhile other patients languish on hospital waiting-lists. The hard-pressed local authority cannot always find accommodation for the "frail ambulant" and mentally unstable patients whom the hospital authorities consider should be provided with hospital accommodation, while the third authority, represented by general practice, though willing to do its utmost to keep the old people well at home, is frustrated if hospital and local authorities fail to provide the help so necessary in medical and social emergencies. The subcommittee quotes with approval a statement by Dr. Mortimer O'Sullivan[2] that whatever the future of medicine in this country the chronic sick and aged infirm will in the main be the responsibility of general practice. "It is hard work, often harassing, and occasionally satisfying."

[1] Bristol Local Medical Committee, 7, The Dell, Westbury-on-Trym, Bristol. 2s. 6d., post free.
[2] *British Medical Journal*, 1952, 1, 1297.

Preparations and Appliances

AN OCCLUDER

Dr. A. ESTCOURT-OSWALD, of Colchester, writes: The occluder illustrated consists of two black disks connected by a small steel clip. The front disk is meniscus in form and the back disk flat. The occluder can very easily be slipped on over one lens of the patient's spectacles, whether they are glazed with flat, toric, or meniscus lenses. The examiner is thus able to test the sight of each eye while both his and the patient's hands are free. I have used this occluder for many years and have found it most useful. It can be obtained (price 6s., post free) from Messrs. Clement Clarke, of 63, Wigmore Street, London, W.1.



Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Modern Treatment

SIR,—A Victorian physician, whose name I have forgotten, used to say that "it took a strong constitution to stand a health resort, a convalescent home, a sanatorium, or an autumn holiday." Were he alive now I think he would add to this list "modern therapy."

Our old friend "treatment" seems to be harmless enough; indeed, I notice that the word is hardly ever used by those clever people who send you articles on the scientific aspects of medicine—articles most of which, I confess, mean almost nothing to me, and, I strongly suspect, to the majority of your readers also. (I note that you hint at this in a leading article in your issue of February 28, p. 496.) No, it is "therapy" which is the danger, and especially modern therapy, to be spoken of in reverential tones and written only in capital letters. I propose to refer to it as M.T. in accordance with the prevailing fashion of obscuring things by calling them by initial letters. M.T. lurks in every doctor's bag usually in the form of tablets or ampoules, but occasionally as a more innocent-seeming lozenge or ointment, and very rarely as a mixture. It accompanies him on his rounds and is ready to jump out at the slightest provocation and grapple with the disease—or should I say the "pathology"?—and it is when there is a tug of war between M.T. and the "pathology," with the patient as the rope, that a really strong constitution is required. M.M. (modern medicine) aids and abets M.T., for, being unable to diagnose the simplest case of "pathology" without numerous investigations, punctures, *x*-ray reports, and specialist opinions, the patient is usually pretty well exhausted before M.T. comes on the scene at all.

I am glad to see from your correspondence columns that the abuse of modern remedies (and their cost) is beginning to be recognized; but I think there should be a new petition in the litany to be read in hospital chapels or wherever doctors and nurses do, or ought to, congregate. It might be as follows: "From inability to let well alone; from too much zeal for the new and contempt for what is old; from putting knowledge before wisdom, science before art, and cleverness before common sense, from treating patients as cases, and from making the cure of the disease more grievous than the endurance of the same, Good Lord, deliver us." I could suggest several more petitions to meet our present needs, but the above may do to go on with.—I am, etc.,

Streatley, Berks. ROBERT HUTCHISON.

Sensitization to Local Application of Antihistamine

SIR,—I was interested to read Dr. W. A. Heaton-Ward's account of a case of sensitization to the local application of an antihistamine (February 21, p. 455). A similar though more dramatic case happened only a few days ago in the routine of our practice.

A healthy young man who, apart from a period of observation for suspected pulmonary tuberculosis earlier in his life, gave no history of previous chest illness developed coryzal symptoms with marked acute rhinitis. He was given "antistin-privine" inhalant to relieve this latter symptom. About five hours after his first inhalation he developed a tightness in the chest. I saw him about 12 hours after the onset of this and found him in a typical, though slight, attack of bronchial asthma. The symptoms rapidly subsided after taking ephedrine ½ gr. (32 mg.) three times daily. Twenty-four hours later the chest was almost clear.

In this case it would appear that the inhalation of an antihistamine spray produced a sharp allergic response in the form of bronchospasm.—I am, etc.,

Hereford. A. DERRICK ROSE.

SIR,—I was interested in Dr. Heaton-Ward's report of a case of dermatitis following the use of phenindamine hydrogen tartrate ("thephorin") ointment (February 21, p. 455). Antihistamine creams and ointments are now widely used in the treatment of various itching dermatoses. For most of these conditions they are contraindicated, and in the remainder they are of doubtful value. In a controlled trial Baldridge[1] found that the addition of a histamine antagonist did not increase the antipruritic action of a vanishing-cream base.

The fact that a substance is capable of neutralizing histamine does not, unfortunately, prevent its being a potential cutaneous sensitizer, and it has been estimated[2] that 2–6% of patients so treated develop eczematous reactions. Sidi *et al.*[3] report that a third of their recent cases of dermatitis medicamentosa resulted from sensitivity to antihistamine creams. Several of these patients became photosensitive, and those sensitized to promethazine hydrochloride ("phenergan") tended to give cross-reactions to the sulphonamides, paraphenylene diamine, and other substances of similar chemical structure.—I am, etc.,

London, W.1. HAROLD WILSON.

REFERENCES
1 *Arch. Derm. Syph. (Chicago)*, 1951, **63**, 260.
2 *Lancet*, 1953, **1**, 126.
3 *Acta Allerg. (Kbh.)*, 1953, **5**, 292.

Early Diagnosis and Cancer Education

SIR,—The headquarters of the British Empire Cancer Campaign in London have issued to every general practitioner a most useful booklet on *The Early Diagnosis of Cancer*. At the same time each is asked: "Do you consider that the launching of a scheme of lay educational propaganda (by pamphlets, lectures, films, etc.) would be of assistance in securing the earlier diagnosis of cancer and thereby improving the chances of a cure? Please answer Yes or No."

Surely, Sir, such a question is premature, since the practitioner can have no evidence whatever on which to base an opinion. In this country cancer education has only just been started in a very few centres. It would be useless to judge by the methods used in other countries, which may suit the psychology of their own people but would not be suitable in this country. It is to be noted that no one is allowed to have an open mind on the subject—the answer must be "Yes" or "No." So far no such question has been sent to consultants, many of whom see in a week as many cases of cancer as a general practitioner sees in a year. I am glad to be able to report that in this area, where all practitioners and consultants are kept fully informed about the efforts to carry out "Cancer Education," the medical profession seem open-minded, most co-operative, and prepared to try out a scheme for educating the public concerning cancer.—I am, etc.,

York. MALCOLM DONALDSON.

Correct Names for Drugs

SIR,—As one recently qualified, I have followed the correspondence on the cost of prescribing and the use of registered trade names with considerable interest, in view of my own experiences. As a student I was taught by a pharmacologist to avoid the use of proprietary names, especially in examinations. Yet, in a finals examination, I was asked, "What about 'physeptone'?" immediately after I had been talking about amidone (now methadone). When working in the wards as clerk and dresser, I knew that the housemen's prescribing was restricted to drugs and preparations found in the *B.P.*, the *B.P.C.*, the *N.F.*, and the hospital pharmacopoeia (now obsolete). On taking up an appointment as house-surgeon at a non-teaching hospital, I attempted to use only "approved names" where such existed. I found that many of these were quite unknown, and that the nurses did not know these names, but only some proprietary names. I was requested to put the ordinary name in brackets after those "fancy names."

Some of the "fancy names" were sulphadimidine, phthalylsulphathiazole, theophylline, amylobarbitone, and pentobarbitone. The hospital in question is a recognized training school for nurses, and I would have thought it a matter of some importance that "approved names" were known, as there are so many proprietary names for the same substance. Some of those in use—for example, one for phthalylsulphathiazole—were previously unknown to me.—I am, etc.,

Oswestry. F. B. SINGLETON.

Classification of Diseases

SIR,—As co-author of the *Textbook and Guide to the Standard Nomenclature of Diseases and Operations*, I wish to say that your review (November 15, 1952, p. 1082) is an excellent one and we appreciate your comments. However, I would like to clarify two points which your reviewer does not know or understand. I am also associate editor of the *Standard Nomenclature of Diseases and Operations*, and I note that the reviewer made the following statement: "It is regrettable that in their enthusiasm for correlating the two codes the editors of the *Standard Nomenclature* invented numerical subdivisions for some international categories, thereby violating an important recommendation of W.H.O." The editors of the *Standard Nomenclature* worked very closely with the Bureau of Vital Statistics in Washington, D.C., and absolutely no international code numbers were assigned other than those by Dr. Selwyn D. Collins, of the Bureau, and his assistant, Mrs. Louise Bollo. When Dr. Collins and Mrs. Bollo started combining the two nomenclatures they realized there were deficiencies in the *International Statistical Classification* and made provisions accordingly. They considered it important that all *Standard Nomenclature* diseases should have a cross reference to the *International* rather than state that the item was not part of the *International*.

Perhaps, too, the reviewer does not understand the value of the disease service classification in the *Textbook and Guide to the Standard Nomenclature of Diseases and Operations*. The *Standard Nomenclature* is being used by 71.5% of the hospitals in the U.S. and there had not been a disease service classification written since 1927, when the alphabetic nomenclature was in use. Hospitals had been clamouring for a disease service assignment for diagnoses as they were listed in the *Nomenclature*, but the editorial advisory board of *Standard Nomenclature* did not consider it advisable to include the classification, therefore its inclusion in the *Textbook and Guide*.—I am, etc.,

Chicago. ADALINE C. HAYDEN.

Information to Patients in Hospital

SIR,—All of us will agree with Dr. E. B. Grogono (February 14, p. 402) that the end we seek is a sympathy and understanding with our patients. Few of us, however, seem to be sufficiently gifted to attain this end without help, and I feel that any means which will lead towards it should be justified. My method of the printed sheet happens to be one I have found satisfactory. I cannot think that there can be such an objection to the printed word, nor do I believe that there is such a lack of originality in the profession that my "wretched" sheet will be copied to any great extent; it can, at most, be a guide to those who would like to try a similar method themselves. I would like to thank the many who have shown an interest in my sheet and could wish that Dr. Grogono had been amongst the numerous general practitioners who wrote to me asking for a copy.—I am, etc.,

Swindon. GUY ROWORTH.

Against Umbrellas

SIR,—In your columns the haphazard use of "umbrellas" of assorted antibiotics has been properly condemned by Mr. Norman C. Lake (December 13, 1952, p. 1307) and others, and you have stressed the desirability of making exact bacteriological diagnoses when prescribing these substances (December 13, p. 1301). To-day I have received a new invitation to expensive inaccuracy: a manufacturer's brochure about a pill which contains an assortment of anti-anaemic substances—for example, iron, liver, vitamin B_{12}, folic acid, etc. Surely it should be obvious that it is an economy and a refinement to have every clinical diagnosis of anaemia substantiated, and progress controlled, by simple haematological examinations so that unnecessary substances should not be prescribed. It is, unfortunately, not rare to come across a patient with a low colour index who has been receiving liver or B_{12} for years without benefit to himself and at great expense to the National Health Service. Such cases of inadequate diagnosis may become commoner if "multiple" pills, which confuse by giving rise to a partial improvement, become popular. Whatever the type of anaemia, two-thirds of the ingredients are likely to be wasted, since an iron deficiency will not need liver, and a B_{12} deficiency will recover without iron.

The National Health Service cannot afford to pay for these wasted ingredients.—I am, etc.,

London, N.W.11. MAIR E. M. THOMAS.

Aetiology of Bronchiectasis

SIR,—While commenting on the papers of Dr. K. D. Forgan Morle and Squadron Leader Philip W. Robertson on "Segmental Aspiration Pneumonia and Bronchiectasis,"[1 2] Dr. W. S. Davis (February 14, p. 400) asks for information regarding the frequency of a history of an abdominal operation as an aetiological factor in bronchiectasis. In a series of 166 cases (137 adults and 29 children) at the Bedford Chest Clinic,[3] four adults traced the start of their symptoms to a general anaesthetic. In two this was for appendicectomy, in one for cholecystectomy, and in one for the treatment of a war wound.—I am, etc.,

Bedford. N. WYNN-WILLIAMS.

REFERENCES

1 *British Medical Journal*, 1951, 2, 994.
2 Ibid., 1953, 1, 130.
3 *Edinb. med. J.*, 1952, 59, 427.

The General Practitioner and Mass Radiography

SIR,—Dr. F. A. Nash, Mr. B. Benjamin, and Dr. T. J. Lee, in their recent article (February 7, p. 304) describing the facilities for chest radiography offered to general practitioners by the South-west London Mass *X*-ray Service, state that, to be adequate, such a service could only be possible were the available mass *x*-ray units to confine themselves to investigations of this nature. As pointed out in your annotation (February 7, p. 322), this is obviously most undesirable, but it is equally obvious that the chest clinics, under existing conditions of staff and equipment, are incapable of dealing with the number of examinations necessary if the estimated requirement of five examinations per 1,000 patients per month is accepted.

In an attempt to overcome these difficulties in the Blyth (Northumberland) area use has been made of an "odelca" 70-mm. camera unit recently provided at the chest clinic. Although primarily installed to assist in the routine work of the clinic, the unit gave such excellent results that it was decided to make an "open" chest radiological service freely available to general practitioners in the area, Friday evenings and Saturday mornings being reserved for this purpose. As the scheme has only been in operation for about two months no figures can be given, but the response has been most encouraging and averages between 50 and 60 examinations each week. This figure, if maintained, comfortably exceeds the estimated requirement quoted above for the area served. Already a number of cases of active pulmonary tuberculosis in need of treatment have been brought to light in which there might otherwise have been delay in diagnosis.

Practitioners are naturally reluctant to burden the chest physicians with extra examinations unless they have reason to suspect that disease may be present, and many in the area served have intimated that they find the "open" radiological sessions of the greatest possible assistance.—I am, etc.,

Blyth, Northumberland. JAMES M. GILMORE.

A Journal and its Readers

SIR,—Those who criticize the *British Medical Journal* because it fails to please all its readers all the time can have little idea of the duties of an editor of a medical weekly journal. Not only must he hold the right balance between news and views, but he must also decide where general interest justifies his giving any particular scientific paper the benefit of a 78,000 circulation. At the same time, by its sponsorship of a fine series of specialist journals, the *British Medical Journal* admits that there is a field for both types of paper. The question which your leading article (February 28, p. 496) poses is whether general practice is a specialty in its own right, and therefore entitled to specialist journals of its own.

Setting aside the main question, it must at least be admitted that the conditions of work of the G.P. differ substantially from those of other doctors. Alone in the profession, he works regularly by both day and night; it is commonplace for him to be seeing his last patient not at 6 p.m. but at 9 p.m. or even later. The inevitable result is that his reading time is strictly limited. I cannot help wondering whether most G.P.s find time to read the articles with which they are presented each week.

Length in itself is less putting off than a turgid style of writing, which afflicts so many of us when we put pen to paper. Here the best remedy is the ruthless sub-editor; the author who objects to this type of surgery can have little regard for his message, for his readership will vary inversely with his verbosity. So I am ready to welcome any journal devoted to general practice, provided it says what it has to say in as few words as possible. And if it stimulates you, Sir, to further efforts in blue-pencil work, it will have done all in general practice a good turn.—I am, etc.,

London, N.7. STEPHEN TAYLOR.

SIR,—A weakness of many journals intended for general medical reading (cf. leading article, February 28, p. 496) is that the accumulated knowledge of a general practitioner rarely finds expression therein for the benefit of other practitioners, general or otherwise. This does not necessarily reflect on editorial policy, for what an editor does not receive he most clearly cannot publish; and I suspect that he receives few articles from general practice. This would not be surprising. While clinical material and problems abound in general practice, there are many difficulties in taking advantage of them. Time is scarce, and especially time free from interruption. The general practitioner usually has no secretarial assistance, and is often unable to obtain laboratory and other investigations. He may be physically separated from reference libraries, he usually works alone in his surgery, and his work lacks the natural checks provided by registrars, house-men, nursing staff, and laboratory assistants. When a publication is the joint production of a team of workers, it gains in "printability." Even when two heads are no better than one, two witnesses certainly are. In these circumstances an article from a G.P. is likely to lack polish, and this renders publication unpredictable. Whether the *British Medical Journal* would be justified in printing this rather "rough" type of contribution is not for me to say.

I was dismayed to learn that the "Refresher Course" articles and "Any Questions?" cater specially for the general practitioner—as if to say that no other section of the profession needs any refreshing or feels impelled to send in a question. In any case, an article in the "Refresher Course" should be able to hold its place in the *British Medical Journal* on its own merits and should not need to explain itself as being "for the general practitioner."—I am, etc.,

Lowestoft. N. B. EASTWOOD.

SIR,—In a leading article (February 28, p. 496) you remind your readers that the *British Medical Journal* is not for general practitioners, or consultants, or public health officials, or laboratory workers, but that it is a journal which aims at representing the best of British medicine in order to "promote the medical and allied sciences." Such an *apologia pro vita tua* must be accorded universal approbation without lack of agreement that the programme is fully implemented; but I do not think you are comfortably convincing in your further reference to the general-practitioner reader.

I am not, of course, prepared with authoritative figures, but of the 78,000 copies distributed weekly a very large proportion must go to general practitioners or (*pace* your disapproval of the term) average readers. You rightly point out that they are catered for by the inclusion of the "Refresher Course"—a series of articles of practical importance and value. It would appear that, if to this feature are added the answers to "Any Questions?" and occasional synopses in short leaders or annotations, the pabulum for the average practitioner has been fully comprehended.

Yet, in order to forestall any charge of inadequate provision that may be supplied elsewhere, you question if the multiplication of journals which aim at the general practitioner's special requirements is a healthy tendency. It is a tendency, you say, that has behind it the assumption that the general practitioner is intellectually inferior, and he must be reassured to the contrary and be encouraged to keep up to date by reading a journal which tries to put before its readers the whole of medicine, not just part of it. I wonder if the large number of average doctors among the 78,000 will feel flattered or offended by the somewhat condescending and surely gratuitous reassurance that they are not intellectually inferior. If I may venture to express an opinion from their point of view, I apprehend that they read a medical journal primarily to maintain and increase efficiency in practice, although there are, of course, many other details in which they will be interested. But, although one may approbate the enterprise of those who like to acquire knowledge for its own sake, it is practical application, not Utopian idealism, that must appeal to the majority. Is the average doctor expected to read the fifteen pages of research comprehended in the article on "Isoniazid in Treatment of Pulmonary Tuberculosis" (March 7, p. 521)? All medical men, you point out, have the same basic training, so he ought, I suppose, to be fully equipped to wrestle with "Capacity of a Cationic Exchange Resin ('Zeo-Karb 225') in Vivo" (March 7, p. 544). I think he would turn more willingly to the "Assessment of Chlorophyll as a Deodorant" (March 7, p. 541), which is admirably epitomized in a short annotation (p. 554), or to the "Effect of Nikethamide by Mouth in Man" (March 7, p. 547), which occupies only one page. Indeed, he could restrict himself to the last six lines of the article, which state that it has no effect whatever.

It is only right that all the details of such communications as the first to which I have referred should be recorded, so that other workers on the subject may critically examine all the evidence which they may wish to confirm or refute. It is only right that rare pathological conditions should be reported, and that the results of investigations of new drugs should be published. The academic approach towards "keeping up to date" demands an intimate study by those on the staffs of teaching hospitals, by examiners for higher degrees and diplomas, and by the candidates for these distinctions, however much or little they relate to their practice. But the average doctor must and can keep up to date without the impracticable effort demanded by such scientific study. It seems to me that you are in error in deprecating the consideration of his special requirements and particularly in introducing the question of intellectual inferiority.—I am, etc.,

London, W.1. ADOLPHE ABRAHAMS.

Chlorophyll as a Deodorant

SIR,—We have been using as a deodorant in radical mastoid cavities a solution containing nine parts by volume of a 10% solution of chloramphenicol in propylene glycol with one part of a preparation of chlorophyll which is perfumed similarly to the "solution C" of Dr. J. C. Brocklehurst (March 7, p. 541). The presence of "solution C" does not interfere with the destruction of cultures of sensitive organisms by the chloramphenicol, and the two solutions make a homogeneous fluid. The presence of "solution C" does not appear to be an irritant to the surface of the cavity nor to increase the occurrence of otitis externa.

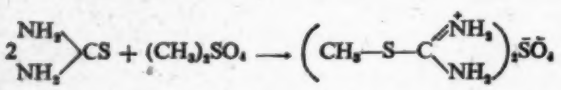
Narrow ribbon gauze, soaked in the chloramphenicol and "solution C" fluid, is used in the cavity and external auditory meatus. The perfume does help to make the smell less unpleasant for the patient and those dressing the cavity, and disturbance of the gauze, by withdrawing the latter slightly, increases its effect. This disturbance (mentioned by Dr. Brocklehurst) and its effect upon odours have long been common knowledge.

We are obliged to Dr. Crawford and Mr. Thompson, Hope Hospital, Salford, for their help.—We are, etc.,

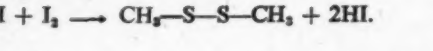
W. B. MCKELVIE.
Manchester, 3. EDITH V. WOODCOCK.

SIR,—With reference to the paper by Dr. J. C. Brocklehurst on chlorophyll (March 7, p. 541), there are certain points with regard to the chemistry of the subject to which I should like to draw your attention.

(1) The formula for chlorophyll, as shown, is incorrect. The two hydrogen atoms attached to the nitrogen atoms of the pyrrole rings should be deleted. (2) Methyl mercaptan cannot be obtained from thiourea sulphate by the action of sodium hydroxide. The standard method of obtaining it is by the action of sodium hydroxide on S-methyl iso-thiouronium sulphate, which is a derivative of thiourea, and obtained by the action of dimethyl sulphate on thiourea :



(3) Methyl mercaptan, in common with other mercaptans, is oxidized by iodine to give dimethyl disulphide and hydriodic acid, which reaction may be represented as follows :



—I am, etc.,

Stockport. H. H. ARMSTRONG.

SIR,—I should like to answer criticisms raised by Dr. W. Mitchell and Mr. L. Deadman (March 14, p. 621) concerning my article on "An Assessment of Chlorophyll as a Deodorant."

The substance referred to as thiourea sulphate is, of course, S-methyl-iso-thiourea sulphate. The method of producing methyl mercaptan gas is that described by Arndt.[1] Chlorophyll (solution "A") was not assayed spectrophotometrically : it was supplied especially for experimental use by a chlorophyll manufacturer, who described the sample as consisting chiefly of sodium copper chlorophyllin. Solution "C," however much chlorophyll it contains, was a true sample of this substance as it is sold to the public. The mercaptan solution used in experiment 4 was a saturated solution of methyl mercaptan in water. Syrup of garlic used in the experiments was the *B.P.C.* compound : this contains aproximately 20% juice of garlic, the composition of which is fully described in the *B.P.C.* monograph. The short time of exposure of methyl mercaptan to chlorophyll in the first two experiments is admitted. The third and fourth experiments were devised to allow a long-continued exposure.

I was interested to read of Dr. Mitchell's experiment with benzyl mercaptan, and look forward to hearing of the outcome of his trials with methyl mercaptan.—I am, etc.,

London, W.12. JOHN C. BROCKLEHURST.

REFERENCE

1 *Ber. dtsch. chem. Ges.*, 1921, **54**, 2236.

Spinach

SIR,—We feel that your expert has not given the whole picture when answering the question on spinach ("Any Questions?" November 29, 1952, p. 1217). Spinach contains 500–800 mg. of oxalic acid per 100 g., more than enough to form insoluble salts with all the calcium and magnesium present in it. Experiments on animals and man have demonstrated the poor availability of calcium in spinach as compared with other greens, milk, whole wheat, etc. Many workers, experimenting with rats, have shown that the oxalic acid in spinach interferes with calcium metabolism, producing increased calcium excretion, considerable calcium deficiency, and consequent poor calcification of bone, deposition of large amounts of oxalates in the kidneys, and formation of urinary calculi and kidney damage. This is particularly so if adequate calcium, magnesium, phosphorus, and vitamins are not included in the diet. Spinach, raw or cooked, when added to the diet of dogs which includes meat, cracker meal, and skimmed milk powder, produces not only a greater negative calcium balance but also poor absorption of nitrogen.

Comparable experiments on children with calcium-deficient diets could not be justified, but it has been calculated that 100 g. of spinach fed to an infant contains sufficient excess oxalic acid to precipitate the calcium in 200 g. of milk, or one-fifth of the total calcium given to the infant. McLaughlin,[1] using spinach as the only food high in calcium in a diet consisting of some of the most commonly used foods, produced positive calcium balances in six out of seven healthy women, but the duration of the experiments was only six days. McClendon and Sedgwick[2] found that the average gain per week was markedly increased when spinach was added to the diets of infants. They used dried and powdered spinach, mixing it with 6% of sea salts. It is possible that excess of salts and consequent water retention had something to do with the weight increase. Sherman and Hawley,[3] on the other hand, were able to show that calcium and phosphorus retention after addition of spinach to the diets of children was in no case as good as with milk feeding alone, while Schlutz *et al.*[4] found, in a six-day experiment, that the use of raw or puréed spinach as a supplement to milk feeding in very young infants did not affect the mineral balance in either direction, but when dried spinach was used the retention was slightly lower than that which prevailed when the minerals were derived solely from milk. Bonner *et al.*[5] fed 10 children aged 5–8 years with 100 g. of spinach for 25 consecutive days, and found that the storage rates for nitrogen, calcium, and phosphorus were not significantly altered. However, they used healthy children, who were fed sumptuously on basal diets which had more than sufficient calcium to obviate any deleterious effect that the oxalic acid of spinach might have produced. It is to be expected that if excess of calcium is present in the diet, particularly in the form of milk, the oxalic acid of the spinach will be neutralized, but what if, as we have sometimes found, children refuse to take their daily quota of milk, and if, as may happen in poorer families, the children are not fed well enough to counteract the effect of spinach in the diet—particularly as it appears that utilization of dietary calcium may be impaired if there is a deficiency of protein in the diet?

Even if there is no upset in calcium balance, calcium oxalate crystals from the ingested oxalates of such substances as rhubarb, spinach, and asparagus are known to cause bladder irritability with frequency of micturition and

occasionally albuminuria and haematuria in man. Spinach also makes the lips of some children red and chapped and the buttocks round the anus red. Is it not possible that the intense dislike of spinach shown by most children is Nature's way of protecting them from its harmful effects? And yet we know of conscientious mothers who have forced large quantities of spinach on their unwilling children day after day.

Are the useful constituents of spinach irreplaceable? We think not. Many workers have pointed out that the cooking or canning of spinach entails a loss of vitamin C—12% by steaming for eight minutes, 60–65% by canning, and over 95% by cooking in a saucepan at 100° C. for 10 minutes. In our experience boiled or canned spinach is generally used in this country. Besides, even slightly wilted leaves will have lost much of their vitamin C before they reach the saucepan. Is it not better to rely on foods which need no cooking?

The use of spinach became widespread when it was shown that it contained large amounts of iron, but it was soon established that for most foods there was no correlation between the total amount of iron and its availability, and that only by feeding experiments could the availability of iron in individual food materials be accurately ascertained. Such experiments on animals have shown that the iron of whole wheat and wheat bran is equal in availability to ferric chloride, followed by beef and pork liver, soya beans, and peas (60% availability). There is little to choose between spinach, beef muscle, and egg yolk (20–40% availability). Spinach feeding is known to have only a moderately favourable effect on Hb formation in anaemic dogs, for the addition of iron salts to the spinach gives a summation effect, indicating that the spinach effect is not due to the iron in this vegetable.

It is of interest that Davidson *et al.*[6] have established clinically the necessity of having calcium-rich diets if a normal blood picture is to be maintained on a diet with a moderate amount of iron. This finding, if applied to spinach, might result in the following train of events in the body: the excess oxalic acid will combine with calcium at the expense of the phosphorus, and the phosphorus thus released will combine with iron, forming insoluble iron phosphate, thus reducing the availability of iron. It is unlikely that vitamin A (or carotene) will be deficient in children's diets if the recommended dose of cod-liver oil or substitute is given, and if foods such as carrots, tomatoes, bananas, beans, brussels sprouts, eggs, and liver are included in the diet.

May we then suggest that, until further light is thrown on the subject, spinach should be considered a doubtful article of diet for children?—We are, etc.,

J. E. BAMJI.
N. S. BAMJI.

London, N.6.

REFERENCES

1. *J. biol. Chem.*, 1927, 74, 455.
2. Ibid., 1921, 46, xxvii.
3. Ibid., 1920, 49, 21.
4. *Amer. J. Dis. Child.*, 1933, 46, 757.
5. *J. Pediat.*, 1938, 12, 188.
6. *British Medical Journal*, 1933, 1, 685.

Feeling the Cold

SIR,—Your annotation on "Feeling the Cold" (February 21, p. 445) tells us that "cold and warmth are separately appreciated. Different points on the skin respond either to cold or to warmth."

A homely experiment leads one to believe that the perception of a temperature gradient on the surface of the body is one thing, while the realization of whether we are dealing with a hot or cold agent is quite another. The experiment is the pleasurable one of lying extended in a warm bath. If the toes are extruded and the cold tap is turned gently on, the sensation is instantaneous, yet one has to tell oneself that the extraneous agent is a cold one; the actual sensation, for me at any rate, does not differ from that produced by a stream of hot water on a cold foot. Temperature gradients, like ionization gradients, find a quick response by the body, but the mind does not immediately register the agent.—I am, etc.,

Bognor Regis. SIDNEY RUSS.

Impetigo Contagiosa

SIR,—The bacteriology of this common condition is worthy of further study. It is an example of the unusual, but not unique, state of affairs in which a reasonably uniform syndrome appears to be associated with either or both of two very different organisms, both of which may also be present as harmless commensals in the body. Here are a few more figures to put alongside those of Dr. R. E. Church and his colleagues (February 7, p. 334):

During 1948 swabs were examined from the lesions of 39 patients with impetigo. None of these patients had received treatment with antibiotics or sulphonamides. The results were as follows:

	Occasions Grown
Staphylococcus pyogenes (coagulase positive) alone	18
β-haemolytic streptococcus alone	6
Staphylococcus pyogenes + *β-haemolytic streptococcus*	12
Staphylococcus pyogenes + diphtheroid	1
Staphylococcus pyogenes total	31
β-haemolytic streptococcus total	18
Other organisms (corynebacterium)	1

The haemolytic streptococci were not all of the same group. The question immediately arises: When A infects B with impetigo and a staphylococcus or streptococcus or both is recovered from the lesions of both patients, are the organisms identical in the two cases? In other words, is the streptococcus the infectious component, preparing the ground for secondary invasion by an indigenous staphylococcus, or is the staphylococcus the continuous factor and the streptococcus the indigenous secondary invader? Or do both organisms when present take part in the serial transmission? There is, of course, another possibility—namely, that some third factor is responsible for the case-to-case transmission, both streptococci and staphylococci being secondary invaders.

On the few occasions on which it has been possible for us to examine the streptococci when impetigo has been transmitted inside a family these have been of the same group and type in all the cases. We have not yet examined the phage type of staphylococci in similar epidemiologically related cases. Though some people claim to be able to forecast from the appearance of the lesions what organism will be found on culture, I have been unable to do so. Despite the advent of chemotherapy and antibiotics the ebb and flow of impetigo in general practice do not seem to have altered very much during the past 20 years.—I am, etc.,

Cirencester. R. E. HOPE SIMPSON.

The Teaching of Preventive Medicine at Oxford

SIR,—The progress report of the Social and Preventive Medicine Committee of the Royal College of Physicians was published in January, 1953, and was recently a subject for annotation in the *Journal* (February 7, p. 323). In this report there is implied criticism that Oxford is the only provincial school without a separate department of social and preventive medicine. The purpose of this letter is to point out that there is a small department of social medicine and that in any case Oxford medical students do get a sound education in preventive medicine. The report gives details of the main topics dealt with by teaching departments of social and preventive medicine, and, with one possible exception, all appear to me to be covered in one way or another in the Oxford curriculum.

In the report, progress is measured by the number of hours allocated throughout the course to direct instruction in social medicine, but is this necessarily a reliable estimate of the total volume of preventive medicine teaching? Surely, we must all

agree that, ideally, each clinician should include preventive medicine as an essential part of his teaching, and that the nearer we can get to this ideal the less is there a need for a special department to cover the subject. From my knowledge of the consultant staff of the teaching hospital in Oxford and the close collaboration which exists between the health department and the special hospital departments dealing with obstetrics, paediatrics, otolaryngology, ophthalmology, orthopaedics, mental diseases, chest diseases, venereal diseases, dermatology, etc., I have no hesitation in stating categorically that the volume of preventive medicine teaching carried out in Oxford by the consultant staff, both by practice and precept, is very material, and Oxford medical students are most fortunate in this respect. In addition, the medical officer of health is also consultant in infectious diseases to the United Oxford Hospitals, so that in my infectious diseases course I am able to combine epidemiological and clinical instruction. Any gaps in this preventive medicine teaching by the consultant staff were filled, until recently, by the staff of the Institute of Social Medicine and will, I am sure, continue to be very adequately filled by the new reader in social medicine.

In addition to the preventive medicine teaching given within the hospital, it is of the utmost importance that medical students should have a sound knowledge of the functions of local-authority health departments, so that after qualification, whether as general practitioners or as doctors in hospital, industry, or laboratory, they will be able to co-operate fully with the many health services provided by the health departments in their area. I have therefore tried to give Oxford medical students a sound knowledge of the work of my department, partly by means of a course of lectures (admittedly short, but compensated to some extent by detailed lecture notes), but mainly by a good deal of practical instruction. For some time now, students in small numbers have regularly attended child welfare clinics, where, in addition to the routine work of the clinic, they have received instruction in various immunological procedures, including vaccination. They have also seen something of the work of the school health service, and more recently a series of public health visits has been arranged in which students, in groups of four, have gone out on successive afternoons with health visitors, mental health officers, sanitary inspectors, midwives, and district nurses (Warin, J. F., *Supplement*, September 20, 1952, p. 133). In connexion with this public health instruction, the report states that "in almost every school the former public health courses have been replaced by modernized courses in social and preventive medicine"; in Oxford it could be claimed that the reverse has also occurred in that a former course in social medicine has been replaced by a modernized course in public health. Perhaps Oxford is leading the way rather than lagging behind, as is inferred in the report.

The advantages of the development of statistical departments in close association with departments of social medicine is rightly stressed in the report, and certainly medical students should have a knowledge of statistical method, but care must be taken that the statistical tail does not wag the social medicine dog. Recent experience in Oxford demonstrated that you can have too much of a good thing, and the students showed signs of acute statistical indigestion by rebelling against the whole course in social medicine.

In the report, and in this letter, the terms "preventive medicine," "social medicine," and "public health" have all been used freely, but neither I nor, I think, anyone else knows precisely what is supposed to be the difference underlying these three terms. Is it not time that there was general recognition that, in actual fact, there is no fundamental difference and that it would simplify matters considerably if we could all agree to use one term, which I think might well be "preventive medicine"?—I am, etc.,

Oxford. J. F. WARIN.

Dosage of Stilboestrol

SIR,—Mr. J. Beattie in his Refresher Course article (Febrdary 21, p. 447) recommends a dosage of stilboestrol up to 25 mg. daily and increasing again thereafter. As the standard dose of stilboestrol is 0.5 mg. (not 5.0 mg.), the recommended dose seems extraordinarily high—beyond, in my opinion, the dose of toleration. Patients with malignant disease on treatment with stilboestrol seem unable to tolerate a dose greater than 15 mg. daily for very long.

Perhaps Mr. Beattie might think it worth while to make further comment.—I am, etc.,

Derby. E. C. DAWSON.

Cleansing of Anaesthetic Machines

SIR,—One of the manufacturers of anaesthetic ether recently received a complaint from a hospital that the ether supplied to them was below standard and that the patients would not take it. On investigation it was discovered that the fault lay in the bottle of the anaesthetic machine itself, which had not been properly cleaned.

This letter is written on behalf of the makers of anaesthetic ether in the hope that you will publish it and the attention of interested parties will be drawn to the danger of using such machines without old ether having first been removed.—I am, etc.,

Ilford. E. J. FLEETWOOD, Sales Manager, Howards & Sons, Ltd.

"Therapeutic Thorns"

SIR,—Professor D. M. Dunlop's review (February 21, p. 441) of the English translation of the Dutch book *Side Effects of Drugs*, of which we were co-translators, is as ingenuous as the qualities—or lack of them—which he attributes to the work in question, and shows a very narrow appreciation of the labour involved in trying to make an English silk purse out of a foreign sow's ear. As regards his view that the "translators have a somewhat sketchy knowledge of English," he will probably be devastated by the riposte that one of us (W. M. C.) is a brother Sassenach born (Irish, not Scottish) and the other (Ph. V.) is a Dutchman who, although highly appreciative of Mr. Jingle, does not let himself be guided by that worthy in his efforts in the English language.

We feel that Professor Dunlop has not been quite fair in his summary disposal of this book. The author accumulated a vast amount of data which had to be condensed into a volume of handy size. This accounts for the "Jingle" style of writing. Professor Dunlop quite forgot to mention that there is a list of getting on for 2,000 references to the literature, from which the author drew his facts, and references to *Excerpta Medica* were only made when he had not access to the original article. Professor Dunlop's rather insular outlook is regrettable when foreign workers are endeavouring to make their observations available to their English-speaking colleagues. Whatever the shortcomings of Dr. Meyler's book, our job was to translate it, not to rewrite it. The end-result, if not redolent of an Osler or a Lane, is at least intelligible, and the condensed information given, if indeed "odd and alarming," represents a considerable amount of serious research on the author's part into the findings of observers all over the world.—We are, etc.,

Amsterdam. W. MULHALL CORBET. PH. VUIJSJE.

Grease on the Skin

SIR,—Will you allow me a slight squeal of protest at your article "Grease on the Skin" (February 28, p. 499)? You say there that Squire and his co-workers[1] showed that the self-sterilizing effects of the skin depend on the action of fatty acids, mainly the unsaturated ones. I showed this many years ago,[2] and Professor Squire has himself acknowledged my work not only in the paper above referred to but in a letter accompanying reprints of his paper. In this letter he too generously describes his own work as very largely a confirmation of my own. It is, of course, far more than that. He and his colleagues demonstrated that the long-chain fatty acids, especially oleic, extracted from the skin itself are the responsible sterilizing agents, whereas I only deduced this fact from experiments done for the most part on hair fat, which at the time seemed far easier to obtain in reasonable quantity.

I think that the real pioneers of this work on autogenous disinfection of the skin are Brann,[3] who discovered that human hair rarely contains pathogenic organisms and suggested that the fats of the scalp and hair might be lethal to

them; Marchionini and his school (in a whole series of papers in the Swiss and German medical press between 1928 and 1939), who showed the cardinal importance of the "acid mantle" of the skin; and Colebrook,[4] who pointed out how rapidly the haemolytic streptococcus and other micro-organisms disappear from various areas of the skin. None of these workers is mentioned in your article, but I dare say you would argue that it was no part of your intention to give a comprehensive review of the subject.—I am, etc.,

Rochester. J. M. L. BURTENSHAW.

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3 Brann, G. (1928). *Klin. Wschr.*, **7**, 2059.
4 Colebrook, L. (1930). *Interim Report of Departmental Commission on Maternal Mortality and Morbidity, Appendix.* H. M. Stationery Office, London.

"Thorough Overhaul"

SIR,—I was interested in the letter of Dr. Ronald Coldrey and others (February 28, p. 507) concerning the "thorough overhaul." In what follows, I take it the request has been made when nothing is complained of. Otherwise, of course, the doctor does whatever is in his opinion necessary in the way of examination.

I always discourage such requests, as in general tending to increase the unnecessary and time-wasting interest the public is taking in disease, and as being outside the scope of the N.H.S. When it is pointed out to patients making this request that the number of doctors who themselves have such regular examinations must be practically nil, they sometimes see the matter in a different light.

Incidentally, I have discovered that the expression "check-up" is not necessarily synonymous with "overhaul," and is often used when the patient has signs or symptoms and desires to be treated for or reassured about them—which is the correct time for him to consult a doctor.—I am, etc.,

Stockport. T. J. KIRKPATRICK.

Smoking and Lung Cancer

SIR,—Dr. R. Doll and Professor A. Bradford Hill (February 28, p. 505) have given an admirable reply to Professor R. D. Passey (February 14, p. 399) but not, I think, entirely disposed of the point he was making. He expressed concern, shared by others, about the effect which some of the wilder statements being made about the results of this work may have on the public. The extent of the real increase of this disease in the last 40–50 years is unknown. Over 80,000 people are now recorded as dying each year in this country from respiratory diseases; about 17% of these deaths are registered as due to pulmonary tuberculosis and about 17% to lung cancer. Smoking would seem to be one of the most important predisposing factors in the development of these tumours, but it is certainly not the only one. It is important that we keep our sense of proportion and remember our responsibility to the public, in whom fear of cancer is already a serious problem.

Doll and Hill have done a fine piece of work and submitted a reasoned and balanced view; others who have not done the work should consider whether the remarks they make about it are helpful and what impact their statements may have on an anxious and ill-informed public. The letters from Dr. H. Binysh and Dr. Lennox Johnston (February 28, p. 505), for instance, do not seem to me to add anything of value. It is, contrary to Dr. Binysh, quite legitimate to suggest that the diagnosis of lung cancer has changed in the last 10 years. Antibiotics have made a clear difference, and this controversy alone is changing it still. It is unjust to infer that Professor Passey dismissed the relationship between smoking and lung cancer as of no account. It is difficult to see how Dr. Johnston can "call on the nation to stop smoking now" without doing more harm with his drama than could be compensated for by any gain over the more prosaic, gradual, and realistic methods of enlightenment which are being adopted.

There are, amongst others, two pieces of information which might be welcomed by the present generation of doctors as they wait for their deaths to round off Doll and Hill's experiment. First, whether the proportion of metastases found in the brain which are due to lung cancer changed with the years from the 30–50% found in the 1920s and 1930s (Elkington[1]). This proportion was thought to be remarkable despite the propensity of bronchial carcinomas to dissemination because of the view then held of the relative infrequency of primary tumours at this site. Secondly, whether the smoking habits of patients developing carcinoma of the larynx, with its falling recorded death rate, are really similar to those of patients with lung cancer (Jacobsson[2]), and, if so, what this may mean.—I am, etc.,

London, S.W.3. D. W. SMITHERS.

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Intercourse after Syphilis

SIR,—Much has been written already on the topic of marriage after syphilis, but, as a most startling statement has been made in a section of the *Journal* ("Any Questions?" January 10, p. 115) which aims at answering questions and avoiding controversial matter, it is felt that it should be ventilated more fully so as to minimize any damage which may have been done. The criteria of cure for early syphilis have remained quite unaltered since the newer and simpler treatments have been evolved. It always has been impossible to be sure of the cure of early syphilis until adequate follow-up procedures have been conducted for at least two years following proper treatment. To my knowledge no one writer, American or otherwise, accustomed to dealing with large numbers of these infections has shifted from this viewpoint, or is likely to.

However, the question of matrimony after syphilis is rather different from the mere granting of permission to have sexual intercourse, for this conjures up the rather novelette situation of a Dorian Gray contemplating marriage to the vicar's daughter. In practice quite another state of affairs usually exists, and the decision regarding marriage is often made on social grounds rather than on those which are entirely medical. Thus, the syphilis may have been acquired from the girl in the first place, in which case both partners will already be under treatment, and, if marriage is still contemplated, sexual intercourse will continue whether the doctor "allows" it or not. Or the fiancée, although apparently uninfected, may be pregnant. In which case she probably has to be examined as a contact and given prophylactic treatment, but certainly not necessarily discouraged from immediate marriage, even if the man has not yet completed his injections.

The basis for any decision depends on whether or not premarital intercourse has recently taken place, and, at the risk of commencing a further controversy, the cynic might say that in this present day and age it is the rule rather than the exception—it certainly is in the bulk of patients for which such decisions have to be taken. If such intercourse has taken place, then the situation is similar to that when a married man has acquired syphilis. Thus it is essential that the fiancée is examined as a contact, and this means that the man has to own up to his misdeeds and to his misfortune. By this time the damage, if any, has been done, and the woman must either be observed to see whether she develops the infection (fifty–fifty chance), or given prophylactic treatment and observed subsequently for *two years* as if she had actually had the disease.

These events at once entail that the female re-examines the question of marriage. If she still wishes to proceed, provided that both parties are aware of the risks which may result from relapse in either, and both attend regularly for observation to safeguard them, and avoid pregnancy, then to advise that they wait even six months is unrealistic, as the patients will not heed the advice. On the other hand, when no intercourse has occurred, and when the

girl is unaware of the situation, to recommend that a man who has had early syphilis may get married after only six months from the initiation of treatment is out of step with all our knowledge of the condition.—I am, etc.,

London, W.1. R. R. WILLCOX.

POINTS FROM LETTERS

Dr. Hugh Welch Diamond

Dr. J. B. WRATHALL ROWE (Harrow) writes: The above-named doctor, who died at Twickenham in 1886, was a pioneer in the field of medical photography and photomicrography. He contributed to the Royal Society in 1856 a paper entitled "The Application of Photography to the Physiognomic and Mental Phenomena of Insanity," and made several photographs of mental patients to illustrate his paper. Although the original paper is still preserved in the Archives of the Royal Society, the photographs have disappeared. I have already obtained from the Royal College of Surgeons, the Medical Society of London, and the Royal Photographic Society information and material regarding Dr. Diamond, but am anxious to trace his original medical photographs if they are still in existence. I should therefore be most grateful if anyone having knowledge of, or early examples of, Dr. Diamond's work would write to me c/o The Medical Department, Kodak Ltd., Harrow, Middlesex. In the library of the Royal College of Surgeons there is a photograph of a mental patient taken by Dr. Warren Hastings Diamond, who may have been the son of Hugh Welch Diamond. Hugh W. Diamond is believed to have had a grandson named R. Hugh Clarke. Any information regarding these persons or their descendants would also be gratefully received.

Alternative to Postgraduate Courses for General Practitioners

Dr. J. B. BAMFORD (Ely) writes: As an alternative to the usual postgraduate course at a teaching hospital, I suggest that the general practitioner could apply to his old teaching hospital, or other central body, for a senior registrar to come and spend a week in his own house. The advantages to both, in my opinion, would be great. I feel that more medicine and more tips are learnt over a cup of coffee or glass of port in the evening than by attending any number of postgraduate lectures. The registrar would also have the advantage of seeing how a general practitioner works and possibly make useful contacts, and would undoubtedly see a number of interesting and rare cases. The general practitioner would be able to obtain another opinion on many of his undiagnosed cases. A registrar could surely be spared by his chief at hospital for one week, or possibly two, in a year. A general practitioner could apply for this visit once in every three or five years. . . . I will be interested to hear what other general practitioners and registrars think of this suggestion and how to put it into operation.

Cancer in General Practice

Dr. W. A. MACKAY (Southport) writes: Your reviewer of this book (February 14, p. 381) passes without adverse comment the statement that in spite of all forms of treatment 50% of cases with stage 1 carcinoma of the breast die in five years. This conclusion is at variance with the report of Sir Gordon Gordon-Taylor to the B.M.A. meeting at Plymouth 15 years ago of 84% survival at ten years. Is the practitioner to conclude that Gordon-Taylor's figures were "optimistic," that cancer is becoming more malignant, or that treatment of cancer of the breast is deteriorating?

Medical Evidence in Court

Mr. J. H. C. PHILLIPS (Northampton) writes: In giving medical evidence it is all too easy to be unintentionally misleading by inference, but I feel that one cannot stress too strongly the grave responsibility of a medical witness in giving the court the benefit of his specialized knowledge, not only to be factually correct, but to be most careful not to imply more than was intended by failure to qualify his statements when necessary. In particular, it is important that witnesses, however eminent, who practise in one particular specialty should neither by direct statement nor by implication give evidence that goes beyond their competence.

Ferrous Sulphate Tablets

Dr. L. F. BECCLE (South Woodford, Essex) writes: I wonder why ferrous sulphate tablets are so freely prescribed for so-called anaemia. In three recent fatal cases of poisoning in infants with which, as a coroner, I have dealt in the last few months, no laboratory investigations whatsoever appear to have been made as to the existence or otherwise of anaemia. What makes the situation worse in my opinion is the utter uselessness of ferrous sulphate in any other conditions. These bright green sugar-coated pills form an irresistible attraction to young infants, who devour them with great relish, with the most unfortunate consequences. What the answer to this menace is I do not profess to know at the moment. I am merely stating facts in the hope that this letter will direct the attention of doctors to this important matter and perhaps influence some to the extent of a little more circumspection in their prescribing of this drug.

Smoking and Lung Cancer

Dr. W. A. BELLAMY (Aylesbury) writes: Dr. Lennox Johnston's outpourings (February 28, p. 507) require an answer. He says, "The performance of our duty . . . is clearly to call on the nation to stop smoking now, voluntarily in the first instance." The magnitude of such a task, even if we as a profession agreed to participate, is so great as to be quite impracticable. And I do not like the implication in "voluntarily in the first instance." I hope, for his sake only, that Dr. Johnston is not suggesting that other means be used. He has, of course, alternate methods of raising £613,000,000 obtained last year from tax on tobacco. He should contact Mr. R. A. Butler immediately. "The upsurge in national health and morale" can take care of itself without Dr. Johnston's help. The nation's health has never been better, and its morale was proved in its "finest hour" not so very long ago—and it would be again should the need arise.

Damages Against Casualty Officer

Mr. J. H. ARMSTRONG (Accrington) writes: Having read the information on the case of *Payne* v. *St. Helier Group Hospital Management Committee* (January 17, p. 166), it seems that an important aspect of the matter has been passed over. No mention seems to have been made by the advocates for early operation as to exactly what should have been done having exposed a bruised caecum. Applying general surgical principles, one would leave a bruised but still viable portion of gut alone, apart, perhaps, from applying hot wet towels as in reduced strangulated enterocele, which, however, would scarcely be useful in the case under consideration. If a clearly non-viable area of caecum could have been found at the time suggested for operation it seems impossible that the patient could have remained for so long without operative treatment in the comparatively fit condition described. If, on the other hand, a bruised but viable caecum had been found it seems that the operation would then have been concluded and to have been of an exploratory nature only and to have played no part in the effective treatment.

Catheterization in Retention of Urine

Dr. D. D. MACDONALD (London, N.1) writes: This problem does concern the general practitioner first and the urological surgeon second. Not infrequently, however, a casualty officer is the first, by reason of equipment ready to hand, to relieve this patient of his distress. One does not like to use the catheter immediately the condition of acute retention is ascertained. Provided the patient's general condition and age will allow of such treatment, ¼–½ gr. (11–16 mg.) morphine given intramuscularly and followed by ½–1 hour's rest on a couch under an electrically heated blanket (or in a hot bath) will bring great benefits. The least of these is that passage of the catheter is infinitely easier for the medical attendant and much less uncomfortable for the patient. The warmth tends to relieve the prostatic vascular congestion, the morphine indirectly to relax spasm of the internal urethral sphincter. The combined effect is often sufficient to dispense with use of the catheter, with its risks and discomfort.

The Metric System

Dr. FRANZISKA FISCHER (Rotherham) writes: Dr. C. Langton Hewer (February 21, p. 450) is somewhat horrified at the idea that instead of "1 drachm per stone body weight" one would have to order "3.55 ml. per 6.35 kg." of a certain drug. That sounds terribly complicated, but nobody dreams of putting it like that under the metric system. One would give "0.6 ml. per kg.," or perhaps 0.5 or 0.7 if that was more appropriate. After all, a drachm per stone is an approximate dosage only, though in general it is sufficiently accurate. I often thought that to put the literal equivalents of the English weights and measures in brackets, as is done in the *Journal*, discourages the use of the metric system. These figures look very complicated and may be a deterrent. The appropriate procedure in my opinion would be to put after the English weights not the exactly corresponding amount in the metric system but the amount one would actually order. If a weight is accurately given in stones, pounds, and ounces, then an accurate equivalent is, of course, required; but it would be much more helpful to put 0.015 g. or 0.01 g., or, if you like it better, 15 or 10 mg., for ¼ or ⅙ gr. than 16 or 11 mg.

Obituary

W. JOBSON HORNE, M.D., M.R.C.P.

Dr. W. Jobson Horne, who died at Mereworth, near Maidstone, Kent, on March 7, at the age of 87, made important contributions to the advance of laryngology, mainly with reference to tuberculosis of the larynx. He was one of the last links with the older generation of laryngologists, for he missed the expected appointment in the 'nineties to the throat department of St. Bartholomew's Hospital because he had taken the M.R.C.P., as was usual in days gone by, instead of the more modern F.R.C.S., which had just become essential.

Walter Jobson Horne was born on August 2, 1865, and educated at Tonbridge School and Clare College, Cambridge, where he took a first class in the Natural Sciences Tripos in 1887, and went on to St. Bartholomew's Hospital, graduating M.B., B.Ch. in 1892, and proceeding M.D. nine years later. He took the M.R.C.P. in 1896, and was awarded the Weber-Parkes medal of the College in 1903. After holding a number of house appointments at Bart's he became chief assistant in the throat department there, and then continued his study of laryngology as a postgraduate at the University of Berlin. In 1896, when the Metropolitan Ear, Nose, and Throat Hospital was reorganized by Hemington Pegler, Jobson Horne joined the staff and began a long connexion with the hospital, which he served not only as honorary surgeon and later consulting surgeon but as honorary treasurer for many years to the board of management. He made his reputation rather as a laryngological pathologist than as a clinical laryngologist, and was the first to point out, by means of serial microscopic sections, that in tuberculous laryngitis the infection could begin in the laryngeal ventricle as well as in more obvious areas. Nevertheless, he was the inventor of two of the most useful and practical adjuncts to otolaryngology—the Jobson Horne ring-probe and the Jobson Horne head-mirror, both favourably known all over the world.

Jobson Horne was honorary secretary and editor of the catalogue of the museum of the British Congress for the Prevention of Tuberculosis in 1901. Having been honorary secretary and vice-president of the Section of Laryngology of the Royal Society of Medicine, he became president of the Section in 1920–1. He was the third laryngologist, following McBride and Killian, to be invited, in 1921, by the University of London to give the Semon Lecture, instituted in 1913 (no lecture was given during the years 1915–20). His lecture was entitled "The Relationship of the Larynx to Pulmonary Tuberculosis," and emphasized the fact, not then universally recognized, that tuberculous laryngitis was always secondary to pulmonary tuberculosis. During the war of 1914–18, when his hospital became the ear, nose, and throat subsection of Millbank (Queen Alexandra's) Hospital, Jobson Horne took a prominent part in the care of aural casualties, and wrote on gun deafness and its prevention. After the war he became aural specialist to the Ministry of Pensions for a number of years.

A B.M.A. scholar in the years 1902 and 1903, Jobson Horne continued to take an interest in the affairs of the Association; he was chairman of the Marylebone Division in 1927, and he held various offices in the Section of Laryngology and Otology at a number of Annual Meetings, being president of the Section in 1924, when the Association met at Bradford. He also served for two years on the Science Committee. His colleagues in London had seen little of him since he retired from practice on the outbreak of the last war. A man of wide culture and recondite knowledge, he was interested in the history of medicine, had been vice-president of the Section of History of Medicine of the Royal Society of Medicine, wrote in its *Proceedings* on St. Blaise—the patron saint of laryngology—and had a notable collection of old lancets. He was unmarried, and in his retirement he enjoyed the rustic life in his country home in Kent. His brother had been a famous collector of Italian works of art, and he himself collected old silver and mediaeval antiquities. The stout, lumbering frame of Jobson Horne concealed a worldly wisdom and a quick intelligence that have left their mark in laryngology.—R. S. S.

G. A. RYRIE, M.B., Ch.B.

The news of the death of Dr. G. A. Ryrie at Kirkcaldy on March 9 at the age of 53 will be received with regret by all those who admired his efforts to make easier the life of those afflicted with leprosy.

Gordon Alexander Ryrie was born in 1899, and was educated at Montrose Academy and at the University of Edinburgh, where he graduated M.B., Ch.B. in 1926. He entered the Colonial Medical Service in 1928, and was sent to Sungei Buloh, in Malaya, to act as medical officer to the leper settlement for three months: he stayed for 17 years. Having overcome the feeling of revulsion which the first sight of the settlement inspired, he accepted the appointment of medical superintendent and held the post until 1945, except for a period of about a year, during which he was a prisoner in a Japanese internment camp at Singapore. As medical superintendent he was responsible for great changes at the settlement. He emptied the leper prison of its inmates and dismissed the armed guards; he was successful in stamping out opium-smoking in the colony; and he improved the general health of his patients by installing modern sanitary arrangements. By the time the Japanese invaded Malaya in 1942 he had had the great satisfaction of seeing the colony transformed from a miserable collection of huts into a model community. The hospital was equipped with modern apparatus, and there were new houses and shops in the village. It was hardly surprising, therefore, that his patients, for whom he worked so hard, should reward him with their love and veneration. It was a bitter blow to him when the Japanese destroyed in a few months all he had built up over a period of 13 years.

After the defeat of the Japanese in 1945 Ryrie returned to Sungei Buloh for a short time, but the hardships he endured during the war and recurrent attacks of malaria greatly weakened his health, and he returned to England. In 1947 he was appointed medical secretary to the British Empire Leprosy Relief Association in succession to Dr. Ernest Muir, and he held the post until the end of 1950, when ill-health compelled him to resign the appointment.

We are indebted to Dr. ERNEST MUIR for the following appreciation:

The death of Dr. Gordon Ryrie ends a life of rare usefulness and devotion, with much suffering bravely borne during his last 10 years. A strong individualist and somewhat of a rebel by nature, he found it hard to fit into the usual routine of the Colonial Medical Service, but when appointed

medical superintendent of the new Sungei Buloh Leprosy Colony, near Kuala Lumpur, a job which few would have chosen, he found there a congenial task. For the next 14 years he devoted himself to the service of the victims of that disease, and built up one of the largest and best-equipped leprosy institutions. Ryrie took a deep interest not only in the social but also in the scientific aspects of leprosy. He contributed particularly to the study of the racial differences of the disease as found among Indians and Chinese.

When the Japanese advanced into Malaya in 1942, and most of the European civilians withdrew, Ryrie refused to leave his post or to abandon his patients. He continued to serve them for some two years. Short of food and medical appliances, he had to watch them day by day dying of starvation and slowly rotting away, in spite of all he could do for them. His life was repeatedly threatened, but he was saved by the devotion of the indigenous inhabitants, whose good will the Japanese were anxious to preserve. In the end he was removed to a concentration camp.

Ryrie had a rare facility in writing, and had his sympathy with suffering not led him to become a physician he might have been a successful literary man. During the years at Sungei Buloh his wife took a large share in the welfare work of the colony. When increasing ill-health made it impossible for him to continue in active work, he retired to Mrs. Ryrie's home in Fifeshire. We extend to her our deep sympathy in her loss.

Dr. A. G. BADENOCH writes: Sungei Buloh Leper Settlement in the Federated Malay States, beautifully sited in a closed valley, contains a central hospital and offices, playing fields, recreation rooms, a small theatre, and a school. Those who care may grow vegetables or keep poultry or pigs. The separate cottages have each its own flower garden. Unfortunately these amenities counted for little until Ryrie was appointed medical superintendent. Leprosy work had been dominated by the tradition that it was a loathsome and incurable disease: segregation and palliation were the rule. The atmosphere was charged with hopelessness and resentment. Gordon Ryrie changed all that within a few months. Trained in tuberculosis work, his new system gave a sense of security to all his staff, and he showed an example by his personal care of the worst cases, many of whom he dressed with his own hands. He appointed the lepers themselves to nursing, administrative, sanitary, and other duties. He was the friend of every one of his 1,500 patients, and after winning their confidence he set the burdensome routine of treatment on a firm and humane basis, with diagnostic and record centres, operation theatre, and isolation wards. Educational and sports clubs were formed, plays were produced, a magazine, *The Dawn*, was printed. Mrs. Ann Ryrie taught in the school. There was an annual sports day, a weekly cinema show, and the usual seasonal festivities. The whole atmosphere of the place soon changed to one of ordered activity and happiness. A survey showed that many patients had become cured or, as the phrase goes, "burnt out" and non-infectious. When Ryrie offered these their freedom, many pleaded to remain, and jobs were found for them on the outside staff.

When the Japanese invaded Malaya, Ryrie refused to leave his leper patients and stayed, sharing their poor rations and scant supplies. He was suspected of underground activities, and a local Chinese threatened to report him unless a large bribe was paid. Ryrie arranged to hand over the money at dead of night. A sick man already, he kept the appointment, limping on his wife's (international) hockey stick. He also carried dummy money and a syringe of HCN. The Chinese got the latter—and the hockey stick to make sure. This led to Ryrie's removal to a concentration camp. When he was released, though suffering severely from malaria, dysentery, and sores, he skipped the home convoy and trekked in disguise back to his lepers. His death—a result of his voluntary martyrdom in Malaya—marks the passing of a good and faithful servant of humanity.

JOHAN M. HOLST, M.D., Hon. LL.D., Hon. F.R.C.S. Hon. F.R.C.S.Ed.

The death of the Norwegian surgeon Professor J. M. Holst on February 17 at the age of 60 came as a great shock to his many friends, who were accustomed to regard his lithe, athletic figure as an expression of vitality and an index to longevity. The son of the physician Professor Peter F. Holst, of Oslo, Johan Martin Holst was born on June 23, 1892, and began his surgical career as a volunteer in Finland during its war of 1918. Just over 20 years later he was again in Finland, this time in charge of a Norwegian ambulance service in 1939. When Norway was invaded by the Germans in 1940, Holst was appointed chief officer to the Royal Norwegian Army, Navy, and Air Force Medical Corps, a post he held for the rest of the war. He escaped from Norway in dramatic circumstances, and continued to take an active part in the war as an organizer and administrator abroad. In 1930, when only 38 years of age, he was appointed professor of surgery in the University of Oslo and was in charge of a surgical department at the Rikshospitalet. He specialized in surgery of the stomach, thyroid, and lungs, and it was his work on the operative treatment of pulmonary tuberculosis in particular which earned him the international reputation he so richly deserved. Holst was a member of the Scientific Academy of Oslo; the Académie de Chirurgie, Paris; and the Finnish and Swedish Medical Societies. His eminence as a surgeon was recognized by his election to the Honorary Fellowship of the Royal College of Surgeons of England in 1943, the Royal Society of Medicine in 1944, and the Royal College of Surgeons of Edinburgh in 1946; the honorary degree of LL.D. was conferred on him by the University of Glasgow in 1951.

Medical Notes in Parliament

Streptomycin Exports

Mr. PETER THORNEYCROFT, President of the Board of Trade, told Dr. Barnet Stross on March 10 that, so far as he knew, no streptomycin was exported to China and Hong Kong in the first six months of 1950. Dr. STROSS recalled a statement that future exports to China for civilian purposes would be based on the amount exported during that period, and asked for an assurance that the fact that none was exported in that time because we had none to export did not mean that there would be no exports to China. Mr. THORNEYCROFT declined to go further in this direction than pointing out that the export of streptomycin was governed not by the export of that particular drug during the period but by the export of the group of drugs in which it was included.

Vivisection Experiments

The HOME SECRETARY, in a reply to Mr. Peter Freeman on March 12, stated that records were not kept of the number of animals used in vivisection, but the total number of experiments for the years 1885 to 1951 inclusive was 26,511,783, including 7,570 experiments on horses, asses, and mules, and 113,422 experiments on cats and dogs. The figures for horses, asses, mules, cats, and dogs did not include experiments where the animal was killed while still under anaesthesia, since separate records were not kept before 1949; nor did they include certain experiments on cats and dogs in 1940 and 1941, since the records were destroyed by enemy action.

Paying for Health Services

Sir GUY LLOYD asked the Minister of Health on March 12 whether, on all forms issued by his department and handled by the public in relation to the health services, he would cause to be printed a statement to the effect that the health services were not free but that the cost was borne principally by the taxpayer.

Miss PAT HORNSBY-SMITH, the Parliamentary Secretary, replied that, while agreeing that this fact could not be too widely known, she did not think that the form of publicity suggested would be practicable.

Spasticity in Children

Mr. W. T. WILLIAMS asked the Minister of Education on March 12 how many special schools were provided for spastic children by her department and by voluntary organization, what sums were provided for the training and education of such children by her department and how such sums were allocated, and how many children of under 16 years of age were registered as spastics. Miss FLORENCE HORSBRUGH replied that there were no general register of spastic children, and she did not collect separate figures for spastic as distinct from other physically handicapped children. Educable spastic children might be sent by local education authorities to ordinary schools or to special schools for the physically handicapped. There were four special schools in England, of which three were maintained by voluntary organizations, and one by a local education authority, specifically for children suffering from cerebral palsy, and a number of others made special arrangements for them.

Tuberculosis Among Immigrants

Mr. KENNETH ROBINSON asked the Minister of Health on March 12 how long the Standing Tuberculosis Advisory Committee had been considering the problem of tuberculosis among persons taking up residence here from abroad, and what recommendations the committee had made on the subject.

Mr. IAIN MACLEOD said the actual reference to the Tuberculosis Advisory Committee was made in December. He understood it was to be discussed in a few days.

Mr. ROBINSON said there were indications that tuberculosis was being "imported" to a disturbing extent. It was not confined to aliens, as had been suggested recently, but included British subjects from parts of the Commonwealth and from Ireland.

Mr. MACLEOD said he did not quarrel with what Mr. Robinson had said. The wider questions he had raised were under discussion with the Ministry of Labour and the Aliens Department of the Home Office.

Aureomycin Supplies

Dr. SANTO JEGER on March 12 asked the Minister of Health whether, now that aureomycin was manufactured in this country and the limitations on its efficacy were so well known among general practitioners, he would make it more freely available to doctors so that delay is avoided when its use is indicated.

Miss PAT HORNSBY-SMITH, the Parliamentary Secretary, replied that the manufacture of aureomycin in this country still involved bulk importation of the crude drug at considerable dollar cost, and the Minister thought that its issue ought still to be subject to the present safeguards. He was not aware that, under these arrangements, there was any undue delay in supplying this drug to general practitioners in cases where its use was indicated. Since October 1, 1952, 896 applications by general practitioners for the use of aureomycin had been granted. About 5% were refused.

The Births and Deaths Registration Bill, a consolidation measure which has passed the House of Lords, was read a second time in the House of Commons on March 11.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **February 28** (No. 8) and corresponding week 1952.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1953 Eng. & Wales	1953 Lond.	1953 Scot.	1953 N. Ire.	1953 Eire	1952 Eng. & Wales	1952 Lond.	1952 Scot.	1952 N. Ire.	1952 Eire
Diphtheria	27	2	7	0	1	37	3	21	1	1
Dysentery	252	50	124	3		591	56	78	3	1
Encephalitis, acute	9	0	1	0		5	0	0	0	
Enteric fever:										
Typhoid	4	0	0	0	4	3	0	0	1	3
Paratyphoid	2	0	10 (B)	0	0	6	0	1 (B)	0	
Food-poisoning	101	15		1		85	21		0	
Infective enteritis or diarrhoea under 2 years				14	22				10	13
Measles*	30,884	1624	388	101	360	5,734	123	483	152	137
Meningococcal infection	47	5	14	1	6	45	5	25	3	5
Ophthalmia neonatorum	24	4	8	0		40	2	13	1	
Pneumonia†	1,897	83	456	20	13	1,143	50	478	20	3
Poliomyelitis, acute:										
Paralytic	12	2	1	2	4	9	1	1	1	
Non-paralytic	1	0				5	0			
Puerperal fever§	278	23	14	2		218	39	9	2	
Scarlet fever	1,455	88	208	49	78	1,613	141	251	18	55
Tuberculosis:										
Respiratory			153	33				161	29	
Non-respiratory			27	5				35	4	
Whooping-cough	2,746	149	250	68	139	2,648	128	418	103	73

DEATHS in Great Towns	1953 Eng. & Wales	1953 Lond.	1953 Scot.	1953 N. Ire.	1953 Eire	1952 Eng. & Wales	1952 Lond.	1952 Scot.	1952 N. Ire.	1952 Eire
Diphtheria	0		0	0	0	0	0		0	0
Dysentery	1	1		0		0	0		0	
Encephalitis, acute		0					0			0
Enteric fever	0	0	0	0		0	0		0	
Infecuve enteritis or diarrhoea under 2 years	13	3	1	2	0	14		1	0	1
Influenza	314	28	20	1	1	29	6	9	1	0
Measles		1	0	0	0		0	1	0	0
Meningococcal infection		3	1				0			
Pneumonia	578	81	45		8	368	57		18	20
Poliomyelitis, acute	8	0			0	0	0			0
Scarlet fever		0	0	0	0		0		0	0
Tuberculosis:										
Respiratory	131	9	10	1	8	176	24	30	4	14
Non-respiratory		1	5	1	1		3	5	1	4
Whooping-cough	3	0	1	0	3	4	0		2	1
Deaths 0–1 year	284	40	47	12	23	296	32	43	23	13
Deaths (excluding stillbirths)	7,575	1003	754	145	179	6,856	967	796	162	202
LIVE BIRTHS	8,101	1208	914	227	367	8,101	1249	910	234	375
STILLBIRTHS	195	16	21			231	30	28		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

Smallpox in the North Country

Up to March 17 four cases of smallpox had been diagnosed in three men working in a cotton mill at Todmorden, Yorkshire, and in the wife of one of them. One man had died. The cases are as follows:

Todmorden M.B., Yorkshire West Riding.—On March 12 a man aged 45 who had sickened on March 3 and developed a rash on March 7 was admitted to Halifax General Hospital. Here smallpox was suspected, and he was transferred three hours later to the Oakwell Smallpox Hospital. On March 16 there was laboratory confirmation. He had been vaccinated only at the age of 2. On March 15 a man aged 60 and his wife aged 57 were admitted to Oakwell Hospital. The man had sickened on February 28, and a rash, then thought to be chickenpox but now diagnosed smallpox, appeared on March 4. The wife's rash appeared on March 16. He had been vaccinated in infancy and again in the 1914–18 war. She had never been vaccinated.

Bacup M.B., Lancashire.—On March 12 a man aged 51 residing at Bacup but working in Todmorden was admitted to a cubicle at the Florence Nightingale Hospital, Bury, with the diagnosis of scarlet fever. On March 13 petechiae appeared, and the man died. Subsequently smallpox was suspected, and on March 16 there was laboratory confirmation. This man had been unwell with a quinsy since February 28, but was forced to take to his bed with what was probably the onset of smallpox on March 9. He had been vaccinated only in infancy.

In view of the delay in the recognition of the causes of the illness in several of these cases, amounting in one instance to a fortnight, it is very probable that the outbreak will continue.

Infant Mortality by Social Class

The latest *Annual Report* of the Registrar-General for Scotland (1950) contains an analysis of stillbirths and infant deaths according to social class of father. The following figures extracted from a table in the report (p. 47) illustrate how the stillbirth and infant mortality rates increase in relation to social class.

Social Class.	Rates	
	Stillbirths per 1,000 Total Births (Live and Still)	Total Infant Mortality per 1,000 Live Births
I	16·3	25·9
II	22·6	24·2
III	26·4	37·0
IV	29·1	43·9
V	32·3	53·6
Total ..	26·9	38·6

The infant mortality in classes IV and V combined is 93% higher than in classes I and II. The difference between the social class becomes greatest for death rates later in the first year of life, neonatal causes (i.e., in the first four weeks) being only 54% higher in classes IV and V than in I and II.

Infectious Diseases

Falls were recorded in the number of notifications of infectious diseases in England and Wales during the week ending February 28—2,006 for measles, from 32,890 to 30,884; 245 for acute pneumonia, from 2,142 to 1,897; 95 for scarlet fever, from 1,550 to 1,455. The only large rise was 549 for whooping-cough, from 2,197 to 2,746.

The incidence of measles, which in the preceding week had reached the highest level since this disease was made notifiable, declined sharply. The largest falls were 367 in Southampton County, from 1,631 to 1,264; 321 in Lancashire, from 2,150 to 1,829; 268 in Durham, from 897 to 629; 335 in Middlesex, from 2,190 to 1,855; 208 in London, from 1,832 to 1,624; 202 in Warwickshire, from 1,630 to 1,428. The largest exceptions to the decline in the incidence of measles were rises of 196 in Devonshire, from 841 to 1,037, and 126 in Kent, from 1,543 to 1,669. Only small variations occurred in the local trends of scarlet fever, with the exception of a decrease of 50 in Lancashire, where the notifications fell from 260 to 210. The largest increases in whooping-cough were 142 in Lancashire, from 540 to 682, and 69 in Kent, from 49 to 118. 27 cases of diphtheria were notified, 11 more than in the preceding week. The chief features of the returns of diphtheria were rises in Lancashire from 2 to 7 and in Warwickshire from 0 to 4. The largest centres of infection were Liverpool C.B. 5, Plymouth C.B. 4, and Birmingham C.B. 4.

13 cases of acute poliomyelitis were notified, and these were 13 fewer for paralytic and 1 fewer for non-paralytic cases than in the preceding week. Huntingdon, with 2 cases, was the only area with more than one case.

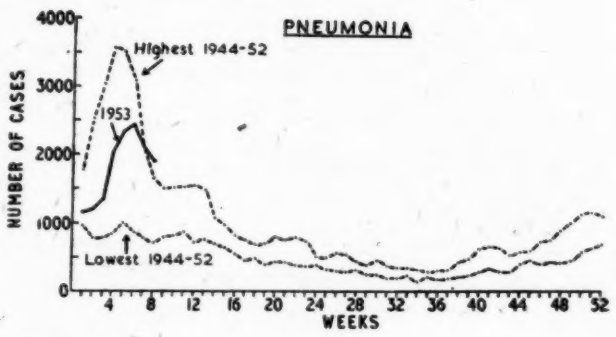
The notifications of dysentery rose from 241 to 252. The largest returns were Lancashire 58 (Liverpool C.B. 20, Manchester C.B. 20), London 50 (scattered through 16 boroughs), Yorkshire West Riding 39 (Leeds C.B. 29), and Warwickshire 14 (Rugby R.D. 12).

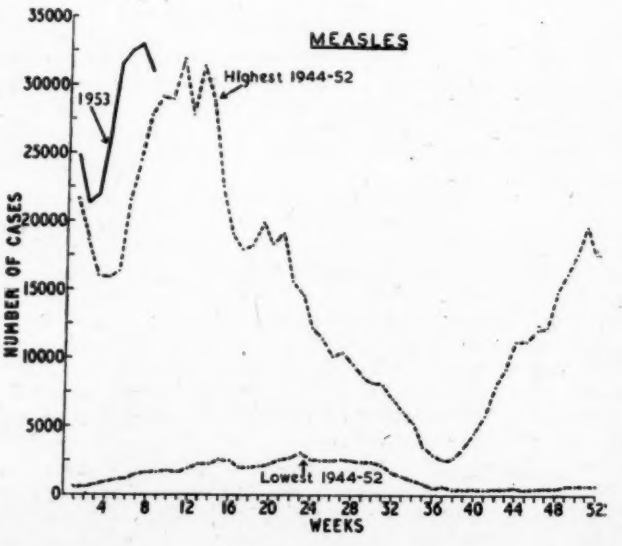
9 of the 10 cases of paratyphoid fever notified in Scotland were reported from Banff County.

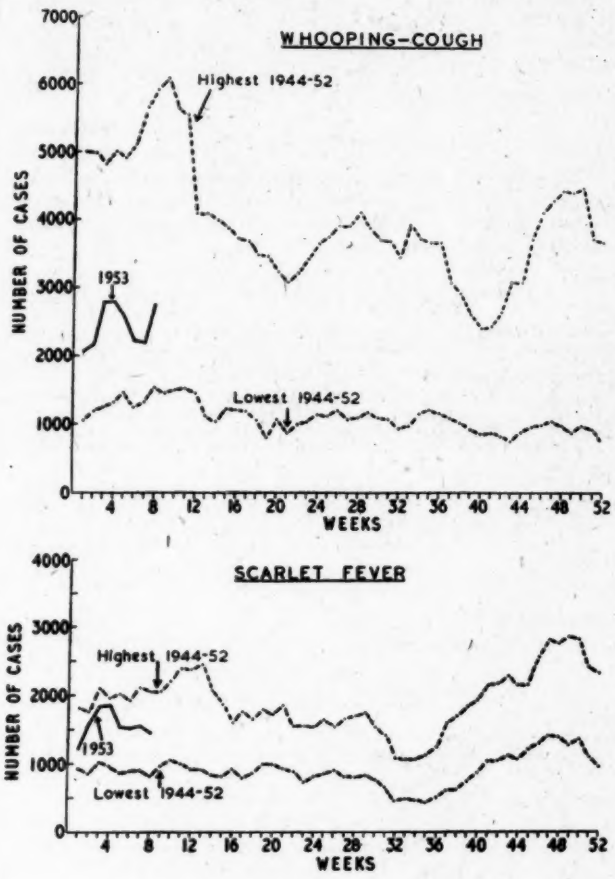
314 deaths were attributed to influenza during the week in the great towns, 207 fewer than in the preceding week.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1944–52 are shown thus -------, the figures for 1953 thus ————. Except for the curves showing notifications in 1953, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.







Week Ending March 7

The notifications of infectious diseases in England and Wales during the week included scarlet fever 1,534, whooping-cough 2,758, diphtheria 22, measles 27,638, acute poliomyelitis 17, dysentery 289, paratyphoid fever 6, and typhoid fever 6.

Medical News

Institute of Almoners.—The Jubilee Dinner of the Institute of Almoners was held at the Holborn Restaurant on March 14, with Professor Alan Moncrieff in the chair. In proposing the health of the Institute, Sir Russell Brain said that the Institute had 50 years of great achievement behind it. The almoner had been created by the growing complexity of society. "We doctors," he remarked, "cannot do without you." The almoner was a new form of social consciousness. He looked forward to the time when all non-medical workers in health would join with doctors in a voluntary council to meet the challenge of the welfare State. Miss E. C. Warner, A.M.I.A., in reply, said that 50 years ago the first almoners' committee was formed, and in the course of time this grew into the Institute. In 1903 there were in existence seven working almoners. Now the Institute had over a thousand members, and they were pleased to have been given university recognition by the recent decision of Edinburgh to provide a third-year course for almoners. Thanks, among others, to their chairman, the Ministry of Health had agreed to provide grants to students. A third point she would like to mention was the successful result of the negotiations on scales of remuneration, and in this connexion they owed much to their general secretary, Miss M. Steel. In 1951 a committee was set up to survey the work of almoners, and the report now drawn up had been almost unanimously accepted. "We have," Miss Warren concluded, "a place within the structure of our society. We must increase our recruits and improve standards of training." The toast of the guests was proposed in a most gracious and witty speech by Miss M. B. Streatfield, A.M.I.A., and Miss E. L. Younghusband maintained the high standard of speeches in her response.

Queen Elizabeth College of Household and Social Science.—The granting of a royal charter to the King's College of Household and Social Science, University of London, which is to be known henceforth as Queen Elizabeth College, after Queen Elizabeth the Queen Mother, was celebrated by a luncheon at the College on Campden Hill on March 11. The principal speaker was Lord Horder, who said that the College dated from a modest beginning in 1908, followed four years later by the foundation of the Household and Science Department of King's College for Women, with Sir Cooper Perry as first chairman. In 1916 a diploma and in 1920 a degree were granted in household and social science. Sir John Atkins, the present chairman, was elected to that office in 1922. Now a royal charter had been granted, and the university degree of B.Sc. had been replaced by two new degrees—B.Sc. in Household Science and B.Sc. in Nutrition. No more significant step could have been taken at Queen Elizabeth College, Lord Horder added, than the addition of the subject of nutrition to its curriculum. There were excellent opportunities in this field of research. Dame Caroline Haslett, who also spoke, mentioned the suitability of nutrition as a career for girls. They would find the theoretical and practical training given at the College invaluable.

Pictures, Books, and Music in Hospitals.—Last week Miss Pat Hornsby-Smith, Parliamentary Secretary to the Ministry of Health, opened a one-day conference on "Pictures, Books, and Music in Hospitals" at the Wellcome Research Institution, London. The conference was sponsored jointly by the British Red Cross Society Picture Library, the St. John and Red Cross Hospital Library, and the Council for Music in Hospitals. Lady Falmouth was in the chair. After an introductory talk on the work of the B.R.C.S. Picture Library by Lady Falmouth, the keeper of the Birmingham City Museum and Art Gallery, Dr. Mary Woodall, spoke on "Pictures and Patients." She was followed by Mrs. Harold Raymond, who described the great expansion of the St. John and Red Cross Hospital Library Department, which now caters for 1,500 hospital libraries in Britain as well as for all Service hospitals at home and overseas. Later there was a demonstration on the art of hospital librarianship. The last part of the conference, devoted to music, was introduced by the Earl of Harewood, president of the Council for Music in Hospitals. Dr. S. F. Mitchell described the curative value of music, particularly for those in mental hospitals. The conference concluded with a talk by Mr. Adrian Hill.

Ciba Foundation.—Since the opening of the Ciba Foundation for the Promotion of International Co-operation in Medical and Chemical Research less than four years ago, the Foundation has done much to live up to its title. Perhaps the most useful of its activities are the informal symposia which it holds in London. To these are invited 40 to 50 experts in the subject under discussion from all over the world. Last year there were six of these symposia, three being devoted to endocrinology ("Bio-assay of Anterior Pituitary and Adrenocortical Hormones," "Hormonal Factors in Carbohydrate Metabolism," and "Synthesis and Metabolism of Adrenocortical Steroids"), and three to general subjects ("The Spinal Cord," "Mammalian Germ Cells," and "Chemical Structure of Protein"). The proceedings of these conferences are later published (see our review pages, February 21, p. 440). Last year the Foundation inaugurated a series of exchange bursaries with the Institut National d'Hygiène in France. The bursaries are to allow doctors to pay short visits to France (or England) in order to obtain clinical experience or undertake research. Last year bursaries were awarded to five British doctors and six French. A constant stream of medical and scientific visitors have been accommodated at the Foundation's house

in Portland Place, London, W.1. On an average there were seven guests each night throughout the year, and they came from 29 different countries.

Cambridge University Health Service.—During the year 1951–2 all except 7 of the 2,296 freshmen arriving at Cambridge (99.7%) submitted to mass miniature radiography. Among them were found 15 cases of "possibly active" tuberculosis, five of which were previously unknown. Another five cases were found among the senior undergraduates, though here only about a quarter of those in residence were examined. This failure to take full advantage of the *x*-ray service is disappointing and the College authorities are blamed for not exerting more persuasion. Four seniors who failed to report for *x*-ray examination developed pulmonary tuberculosis during the year. Over three-quarters of the freshmen were also examined clinically (half an hour each), and, although the commonest causes of reference were eye symptoms or bad teeth, the University's major medical problems are said to centre round pulmonary tuberculosis and mental upset—as at Oxford. The health service is analysing its height and weight records of 7,000 undergraduates with a view to preparing standard tables.

Honorary Degrees at Edinburgh.—Among those who will receive the honorary degree of LL.D. at the summer graduation ceremonial at Edinburgh University in July are Professor Charles McNeil and Dr. S. L. A. Manuwa. Professor McNeil is professor emeritus of child life and health in the University of Edinburgh, and Dr. Manuwa is inspector-general of Medical Services, Nigeria. During the bicentenary celebrations of the publication of Dr. James Lind's "Treatise of the Scurvy," which are due to be held at Edinburgh on May 22, Surgeon Vice-Admiral Sir Sheldon Dudley will be made an honorary M.A. Lind recommended the juice of citrus fruits for the prevention of scurvy, and it was largely owing to him that scurvy was eventually eradicated from the British Navy.

New Geriatrics Journal.—The American Geriatrics Society has begun publication of a new journal on its specialty, the *Journal of the American Geriatrics Society*. It will appear six times a year at an annual subscription of £4 2s. The agents in this country are Messrs. Baillière, Tindall & Cox, 7–8, Henrietta Street, London, W.C.2. Interest in this subject in the U.S.A. is already sufficient to sustain two other journals, the quarterly *Journal of Gerontology*, and the bimonthly *Geriatrics*. There is at present no British journal specializing in this subject.

Register of Orthoptists.—The 1953 *Register of Orthoptists* has now been published, and is available free to medical practitioners on application to the secretary and registrar, Board of Registration of Medical Auxiliaries, B.M.A. House, Tavistock Square, W.C.1. Orthoptists are classified on a geographical basis, and the *Register* gives addresses and telephone numbers and denotes where private practice is undertaken.

Public Health (Infectious Diseases) Regulations, 1953.—New regulations on the notification and prevention of infectious diseases come into force on April 1. In general substance and form the new regulations are similar to the old. The main changes relate to the control of food-poisoning: wider powers are provided for its prevention.

Emergency Bed Service: Applications and Admissions.—During the seven days ending March 16 the number of applications made by doctors to the London Emergency Bed Service for admission of patients was 1,336, of whom 87.2% were admitted.

Dr. George Oliver, of Harrogate, in 1904 gave to the Royal College of Physicians £2,000 to endow a lectureship or prize in memory of William Sharpey. The College has not yet been able to obtain a portrait or photograph of Dr. Oliver, and if anyone knows of the existence of one would he kindly communicate with Professor E. C. Dodds, Harveian Librarian, Royal College of Physicians, Pall Mall East, London, S.W.1.

Dr. A. Q. Wells, a member of the Medical Research Council's staff at the Sir William Dunn School of Pathology, Oxford, and an authority on murine tuberculosis, has been appointed a Sheriff of Oxfordshire.

COMING EVENTS

Association of Clinical Biochemists.—The inaugural general meeting of the Association of Clinical Biochemists will be held at 2.30 p.m. on March 28 at the Postgraduate Medical School of London.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, March 23

MEDICAL SOCIETY OF LONDON.—8.30 p.m., discussion to be introduced by Dr. T. H. Mills and Mr. M. A. Falconer: Value of Arteriography.

ROYAL EYE HOSPITAL.—5.15 p.m., Dr. T. H. Whittington: Physiology of Accommodation Clinically Considered. Treatment of the Hypermetrope.

Tuesday, March 24

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. W. N. Goldsmith: Vegetating Dermatoses.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor H. H. G. Eastcott: Arterial Grafting for the Ischaemic Lower Limb.

WEST END HOSPITAL FOR NERVOUS DISEASES.—5.30 p.m., Dr. N. G. Hulbert: Neurological demonstration.

Wednesday, March 25

BIRMINGHAM MEDICAL INSTITUTE: SECTION OF PSYCHIATRY.—At Monyhull Hall, King's Heath, 8 p.m., clinical meeting.

EUGENICS SOCIETY.—At Burlington House, Piccadilly, W., 5.30 p.m., Dr. Gertrude Willoughby: Population Problems and Family Policy in France.

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. H. Haber: Lichenoid Eruptions.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, W.C., 4.30 for 5 p.m., Mr. H. G. Hanley: Disorders of Micturition in Females.

ROYAL EYE HOSPITAL CLINICAL SOCIETY.—8 p.m., Mr. M. A. Falconer: Visual Field Changes in Compressions of the Optic Nerve.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Dr. J. B. Alexander: Recent Advances in the Treatment of Pulmonary Tuberculosis in the Adult.

ROYAL SANITARY INSTITUTE.—At Town Hall, Welshpool, 10.15 a.m., Dr. I. J. Jones: Trend of Population and its Effect on Public Health; Mr. F. A. Lodge: Slum Clearance Problems of To-day.

WELSH NATIONAL SCHOOL OF MEDICINE.—At Reardon Smith Lecture Theatre, Park Place, Cardiff, 8 p.m., 4th William Sheen Memorial Lecture by Sir Cecil Wakeley, P.R.C.S.: Modern Trends in the Treatment of Cancer.

Thursday, March 26

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Mycology—Epidemiology of Fungous Infections.

LIVERPOOL MEDICAL INSTITUTION.—8 p.m., Dr. Lennox Johnston: Cure of Tobacco Smoking.

LONDON JEWISH HOSPITAL MEDICAL SOCIETY.—At 11, Chandos Street, W., 8.30 p.m., Dr. M. H. Pappworth: Science of Diagnosis.

MIDDLESEX COUNTY MEDICAL SOCIETY.—At Central Middlesex Hospital, 3 p.m., clinical meeting; 4.45 p.m., Dr. F. Avery Jones: Australian Journey (with colour slides).

NORTH-WESTERN TUBERCULOSIS SOCIETY.—At Manchester Royal Infirmary, 4.30 p.m., Mr. J. F. Dark and Mr. P. Jewsbury: Lung Resection in Pulmonary Tuberculosis.

ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Dr. E. R. Cullinan: East African Interlude.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor S. S. Rose: A Clinical and Radiological Survey of 150 Cases of Recurrent Swellings of the Salivary Glands.

Friday, March 27

BIOCHEMICAL SOCIETY.—At Department of Biochemistry, University College, W.C., 11 a.m., annual general meeting.

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. L. Forman: Lichen Planus.

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES.—7.30 p.m., general meeting. Dr. A. H. Harkness: Therapeutics of Non-gonococcal Urethritis.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Feilden.—On March 5, 1953, at the Roan Antelope Copper Mines Hospital, Luanshya, Northern Rhodesia, to Elspeth (formerly Brown), M.B., B.S., wife of Francis Antony Feilden, a son—Humphrey John.

Howell.—On March 3, 1953, at St. David's Hospital, Cardiff, to Jean, wife of Dr. David Gordon Howell, a son—David Vaughan.

Masters.—On March 8, 1953, at Mason's Hill Maternity Hospital, Bromley, Kent, to Jean (formerly Newland), wife of Edgar James Masters, M.B., B.S., a son—Nigel James.

Sers.—On January 22, 1953, to Dr. Phyllis (formerly Neil), wife of Dr. Rolf Sers, Goldboro, Nova Scotia, a son.

Turner.—On March 3, 1953, at University College Hospital, London, W.C., to Joan, wife of Robert G. Turner, F.R.C.S., a son—Peter.

DEATHS

Buckle.—On February 27, 1953, at 56, Woollards Lane, Great Shelford, Cambridge, William Frederick Buckle, M.D.

Cartwright.—On February 22, 1953, at the Lonsdale Nursing Home, Tunbridge Wells, Kent, Ernest Henry Cartwright, M.D., D.P.H., formerly of Myskyns, Ticehurst, Sussex, aged 87.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

The Origins of Clinical Thermometry

Q.—*When was the measurement of the temperature of the body first used systematically for medical purposes, and when and where was the first clinical thermometer made?*

A.—Hippocrates regarded heat as the chief diagnostic sign of acute diseases. Galileo is generally credited with the invention of the spirit thermometer. Sanctorius introduced it to the medical profession; in his commentary on Avicenna (Venice, 1626) he demonstrated its usefulness in the study of disease. His book includes an illustration of a thermometer. Fahrenheit introduced his scale in 1714, and Réaumur in 1730 introduced a mercury thermometer with a scale of 80° between freezing and boiling points. The centigrade scale was invented by Celsius, of Upsala, in 1742, with 100° as the melting point of ice and 0° as the boiling point of water. In the following year Christin, of Lyons, reversed this scale.

The first accurate observations on the temperature of healthy men and animals seem to have been recorded by G. Martine in his *Essays, Medical and Philosophical*, 1740. Boerhaave used the thermometer extensively in clinical work, probably employing the ordinary weather instrument. In 1835 Becquerel and Breschet established the mean body temperature in health as 37° C. (98.6° F.). The self-registering maximum thermometer for medical use was invented by Aitken about 1865. It was a cumbrous instrument some 10 in. (25 cm.) long, and in 1867 Clifford Allbutt instructed a Leeds firm to make him a series of experimental thermometers, and succeeded in reducing the length of the tube to 3 in. (7.6 cm.). The pocket clinical thermometer thus devised by him came rapidly into general use. The word *thermomètre* first appears in J. Leurechon's *Recréation mathématique*, 1624.

Intermittent Claudication Unrelieved by Sympathectomy

Q.—*What further treatment is available for sufferers from intermittent claudication after the failure of lumbar sympathectomy?*

A.—Conservative measures such as Buerger's exercises and the use of vasodilator drugs such as tolazoline ("priscol") should be persisted with. If there is no improvement a year after sympathectomy section of the tendo Achillis must be considered. This aims at relieving pain in the gastrocnemius and soleus muscles by inactivating them. It may also relieve pain arising in other muscles of the leg by reducing the bulk of muscle demanding blood during exercise. The most suitable cases are those in which pain starts in the back of the calf and radiates upwards or downwards without encircling the leg. A forecast of the possible effect of tenotomy may be made by applying a below-knee plaster cast to fix the ankle, and then observing the effect on walking distance of this method of reducing the activity of the gastro-soleus group. Raising the heel of the shoe on the affected side is sometimes helpful. The most suitable cases for tenotomy are those in which the opposite limb is relatively unaffected and in which the walking distance is less than 50 yards (45 m.). The operation should not be done unless the nutrition of the skin of the limb is good. There is some loss of power in certain actions such as pressing the brake pedal of a car, and this must be considered before operation is decided upon.

Reconstructive operations such as grafting are now possible in highly selected cases in suitably equipped centres. Arteriography is a necessary first step. Localized thrombosis in an otherwise relatively healthy arterial tree may allow the insertion of a graft. The operation is best reserved for patients with more serious symptoms than claudication alone.

Sudden Death after Penicillin

Q.—*Sudden death has been recorded following the injection of penicillin and ascribed to undue sensitivity to it. (1) Should sensitivity-testing be adopted routinely before giving penicillin? (2) What is the medico-legal position if there is a fatality and sensitivity-testing has not been done?*

A.—Sudden death after a penicillin injection is almost unheard of and not explicable as the result of sensitization, when the principal effects are fever and urticaria, although occasionally a shock-like condition may result. Death has been caused by the injection of excessive doses intrathecally and by the accidental penetration of a vein during an intramuscular injection of certain preparations of penicillin other than those ordinarily used, but presumably the question does not refer to such cases. In view of the enormous number of doses of penicillin given daily with no ill effects by practitioners who could not possibly afford the time for precautions to guard against a highly improbable contingency, the answers must obviously be: (1) No; (2) There appears to be no cause of action.

Exact Identification of Bacteria

Q.—*(1) What methods of typing bacteria are now available to assist the study of the spread of disease? (2) To which diseases of man may these methods now be usefully applied?*

A.—(1) Bacteria can be typed by serological methods or by means of bacteriophage. The former are applicable to pneumococci, streptococci, meningococci, staphylococci, diphtheria bacilli, and in a modified sense of the term to certain of the *Enterobacteriaceae*, such as salmonella and dysentery bacilli. The latter is used chiefly for typing *Salmonella typhi, S. paratyphi* B, *S. typhi-murium*, and staphylococci. Methods for typing other organisms by bacteriophage have been described, but are not in routine use.

(2) These methods can be applied to the investigation of any of the diseases caused by the organisms which have been mentioned. In general, serological typing involves a good deal of work, and is reserved for special investigations. Bacteriophage typing of *S. typhi, S. paratyphi* B, and the staphylococci is relatively simple, and is employed as a routine where there is any reason to expect that the information obtained would be of epidemiological interest.

Kieselguhr Powder

Q.—*What is kieselguhr powder? Has it any harmful effect if inhaled or in contact with the skin? A patient is exposed to the powder in his work, and complains that it causes a sore throat and cough.*

A.—Kieselguhr powder is one of the diatomaceous earths, consisting of the skeletons of extinct diatoms. Its composition is almost pure silica in an amorphous form. Because of its amorphous form it is generally regarded as being a harmless dust to inhale. When inhaled in sufficient quantity over a long period of time it can cause silicosis; but whether or not silicosis develops probably depends on the treatment—for example, grinding or crushing—which the kieselguhr undergoes. The powder also has a drying effect on the throat and trachea, causing soreness and cough.

Some authorities state that calcined diatomaceous earths cause silicosis much more rapidly than those not so treated. For this reason it is very difficult to give any specific safe maximum concentration of dust. This type of silica may be mixed with alkalis and soap powders in the manufacture of abrasive cleaners, in which case the action of the silica

on the lungs seems to be increased by the presence of alkali. Apart from its abrasive qualities, which may rarely give rise to a friction dermatitis, the powder should not be harmful to the skin.

Kieselguhr powder should be handled with care. If the method of use is such as to cause continuous clouds of dust, it should be handled under exhaust ventilation. Special care is required in the case of calcined and ground kieselguhr.

Non-operative Treatment of Dupuytren's Contracture

Q.—*Is there any non-operative treatment likely to improve an early case of Dupuytren's contracture? Would splinting during sleep be helpful? The patient's main relaxation is playing the piano.*

A.—There seems to be no doubt that the progress of some cases of Dupuytren's contracture can be delayed, if not arrested, by the wearing of an appropriate splint at night combined with frequent manipulation of the finger by the patient himself during the day.

For many years a search has been made for some internal or local medicament which would soften contracting fibrous tissue. The use of "fibrolysin" and "iodolysin" (thiosinamine derivatives) in this way will be remembered by older practitioners. Recently two further materials have been suggested, the one vitamin E, and the other phenyl-cinchoninic acid. The writer has not noted much improvement from the employment of any of these methods, but some maintain that in the case of vitamin E the doses frequently used are inadequate and that if massive doses are given for a prolonged period results are obtained.

NOTES AND COMMENTS

Asthmatic Attacks in Infancy.—Dr. E. R. WINTON (London, S.E.9) writes: In the *Journal* of January 31 (p. 285) under the heading "Any Questions?" an inquiry was made about the alternative to injecting adrenaline in treating an asthmatic attack in a child. The questioner and his respondent (and perhaps others) might be interested to know that for about a year I have tried an unorthodox method with a modest amount of success. The treatment is to administer sublingually two or three minims (0.12 to 0.18 ml.) of ol. myristicae *B.P.* It had occurred to me that the essential oils used as carminatives, which somehow relaxed the cardiac sphincter sufficiently to permit eructation, might also act on other plain muscles; and an old wives' tale to the effect that nutmegs hung round the neck protected against asthma led me to use the particular oil mentioned as a pilot experiment. The administration of this oil is simple, requires no technical skill as does the syringe, conveys no discomfort in use, and in the dosage employed appears to produce no bad side-effects. If only one could say this of adrenaline, isoprenaline, and like preparations!

As it chanced, my first two cases, a girl of 6 and a woman of 35, were both completely relieved in an attack within a few minutes. In the case of the child I had my stethoscope applied to the chest and a stopwatch in my other hand; all spasm disappeared in two minutes exactly. In a later attack in this same child I had the pleasure of being able to demonstrate to my wife complete relief exactly two minutes after instilling the oil. Subsequently I obtained identical results in a little boy; the rest of a dozen cases either required a further dose after five minutes to obtain fair relief, or were very little helped. One lad of 16 acquired resistance to the treatment over weeks, and had never had relief comparable to isoprenaline or adrenaline; he is now considerably resistant to adrenaline also. In no case was there report of undesirable side-effects; I have myself taken sublingually five times the maximum *B.P.* dose without untoward effect.

My impression from this small, by no means statistically significant group of cases is that the better result may be looked for in young children, and that where irreversible bronchial changes have taken place the drug is likely to be useless. Certainly, of the six adults treated with this oil, only one obtained good relief. The only lesson I draw from this small experiment is that at least one essential oil containing many complex substances happens to contain some ingredient or combination of ingredients which relaxes smooth muscle. There are many essential oils, and a properly conducted clinical investigation combined with a laboratory study of the individual substances contained in them may reveal some useful non-toxic preparations to be added to our armamentarium. And in asthma, at least, this would be very welcome.

OUR EXPERT writes: There are very many unorthodox treatments of asthma, none of which were included in my brief answer. Some of the unorthodox treatments help individual cases by virtue of their ingredients, others work by faith. Most of these unorthodox treatments have been tried by orthodox doctors interested in asthma and have not been found to be helpful in a sufficiently high proportion of patients to be advised generally. Dr. Winton's results are not really surprising, for carminatives are known to help some attacks of asthma in some cases, perhaps rather more frequently than is appreciated in these modern days. The older clinicians some 20 to 30 years ago who emphasized "reflex causes" of asthma appreciated the relief that might be obtained when treatment was directed to relieving or avoiding gastric or colonic distension, but the older physicians were also all agreed on the value of ephedrine and adrenaline when they first came. We must also not forget that an injection of sterile water will sometimes stop an attack of asthma quite dramatically and within a few minutes. Asthma is a psychosomatic disease, and confidence and enthusiasm are assets in its treatment, as they are in many other illnesses.

It is of interest to learn of Dr. Winton's experience, but one would hesitate to conclude that "at least one essential oil containing many complex substances happens to contain some ingredient or combination of ingredients which relaxes smooth muscle." It does not necessarily follow, for an attack of asthma can be relieved by sterile water injection and also by an enema (I have known quite a few children relieved by enema), but in neither case is there any substance with relaxes smooth muscle. One would hesitate to recommend these methods of treatment as a routine. Carminatives have a very slight antispasmodic action, but it is indeed very slight, even though Dr. Winton tends to push up the dose a little high, and large doses can be dangerous.

A PHARMACOLOGIST writes: According to the published statements the treatment of asthma in children with 2 to 3 minims of ol. myristicae is not without risk. The oil constitutes about 10% of the material present in the nutmeg, and the toxic dose of nutmeg is 5–10 g. Hence the toxic dose of the oil may be as low as 0.5 g., and the doctor is giving nearly that dose. He states that he himself has taken about five times this dose by putting it under his tongue. There is great variation in the toxicity of a substance like ol. myristicae for different individuals, and he may be unusually resistant. There was a discussion of nutmeg poisoning in the *Proc. roy. Soc. Med.*, 1908 (Sect. of Therapeutics and Pharmacology), p. 39, and again in 1909, p. 69, in which Cushny and Dale took part. Numerous cases of poisoning by one or two grated nutmegs were described. There is no mention of an action on smooth muscle. There is a reference to nutmeg as a mild and safe hypnotic for children, and Dale thought that this therapeutic use was at least worth considering.

Foot-drop after Delivery.—Dr. W. S. ANDERSON (Brechin) writes: As a comment to the query on this subject ("Any Questions?" March 7, p. 575) may I state that my one experience of this condition was with a patient who developed foot-drop soon after delivery, and who gradually exhibited the signs and symptoms of disseminated sclerosis, from which she ultimately died some 12 years later? The foot-drop was treated, in the first place, orthopaedically.

Allergic Rhinitis.—Drs. MORRIS CUTNER and B. S. SWEETMAN (Chelsea, S.W.3) write: Your expert writes ("Notes and Comments," March 77, p. 576), "I have no personal experience of histamine ionization, but zinc ionization will help about half those with allergic rhinitis." May we just point out that zinc ionization is a localized treatment applied to the nasal mucosa for a localized result, whereas in the former treatment the histamine is ionized into the skin of the forearm and aims at a cure by effecting a general reaction.

"Any Questions?" Book: Second Series.—This is now available, price 7s. 6d. (postage 6d. extra), from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

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